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ROYAL COLLEGE OF SURGEONS OF ENGLAND

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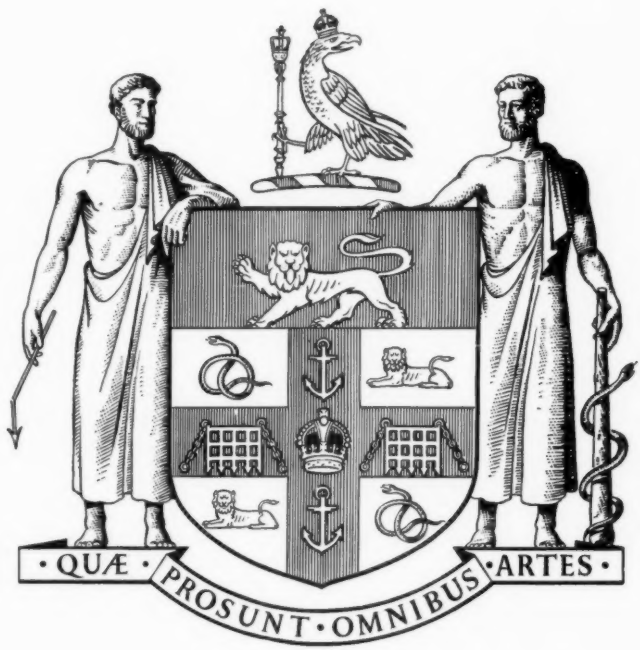

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BARBER-SURGEONS IN GREAT BRITAIN AND IRELAND

Thomas Vicary Lecture delivered at the Royal College of Surgeons of England
on
30th October 1958
by

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Past Master of the Company of Barber-Surgeons of London

I HOPE TO interest you, in this Vicary Lecture for 1958, in the history of some of the Companies and Guilds of Barber-Surgeons in Great Britain and Ireland, apart from our flourishing Livery Company of Barbers, or Barber-Surgeons, of London, of which I have the honour to be the immediate Past Master. I am deliberately leaving out, as far as possible, reference to our London Company [an ancestor of this College], for its history was so fully recorded by Sidney Young, one of our former Masters, in his book *Annals of the Barber-Surgeons of London*, published in 1891.

My interest in Barber-Surgeons goes back to my school-days at Newcastle-upon-Tyne, a city to which I am much attached and where I still have many friends, particularly among the medical profession. I became aware, quite early in my life, that a Company of Barber-Surgeons existed in that city and, indeed, as I shall be able to tell you, still continues to exist. It is therefore not surprising that when I came to work in London, and wished to join a City Livery Company, I chose the Barbers, or the Barber-Surgeons, as they were known for hundreds of years.

Until quite recently, when I was beginning to collect material for this lecture, I believed that the only two surviving Companies of Barbers, or Barber-Surgeons, were in London and Newcastle-upon-Tyne ; and I was quite astonished to learn that there is still another in the city of Chester. All the others came to an end long ago, most of them before 1745, the year when the Barbers and Surgeons in London finally separated.

Few written records remain concerning many of the Guilds of Barber-Surgeons which were once scattered so widely through our country, but fortunately in a few places one or more local doctors, interested in medical history, collected accurate information on the spot before it was too late, and have published lectures and even long monographs. These have been of great help to me in my researches ; and moreover they have often contained references to similar Guilds elsewhere, which I have been able to follow up with the friendly help of city archivists who have access to Freeman's Rolls and other historical municipal documents of their city.

Some of the larger Companies had Royal Charters, confirming them at intervals in their rights and privileges—London and Dublin are good examples—but by far the majority of Barber-Surgeons were simply local

Craft Guilds, subject to the control of the municipal authorities—Mayors, Sheriffs and Council. A Barber-Surgeon became a Freeman of his town or city, and his name and occupation appear in the Freeman's Rolls. Sometimes other valuable information lies hidden among old municipal records such as, for instance, the probate of a Barber-Surgeon's last will and testament, containing the only copy known of the Seal of his Guild.

In various ways I have collected, in the past two years, a large amount of information about Barber-Surgeons, and may still obtain more. I already have almost enough, when properly organised and collated, to make a book—a result which I note has already happened to some previous Vicary Lecturers!

To-day, in a short lecture, I can do no more than attempt to skim off a little of the cream, and provide a list of references from which others, at some future time, may make a start.

Fig. 1. Barber-Surgeons' Hall, Monkswell Street, London. The Hall of the Parent Company.

It is obvious throughout all known records that the London Company was always regarded as the Parent Company (Fig. 1). The Rules and Ordinances of provincial Guilds are mostly, but not universally, close copies of those used in London; and again most, but not all, used the same Coat of Arms and Seal as the London Company (Fig. 2).

It is of interest to note that in a number of cities, but not in London, the Barber-Surgeons were united, apparently from their commencement, with the Wax and Tallow Chandlers (sometimes one, sometimes both) to form a single Guild; and everywhere, when the wearing of powdered

wigs by males became fashionable, the art and craft of Periwig Maker was added to the professional work of the Barber-Surgeons.

Fig. 2. Coat of Arms of the Barber-Surgeons of London.

The origin of Guilds (or Gilds) in Britain

There is material already published in many volumes, and I would refer especially to the works of Toulmin Smith, Malet Lambert and to the full accounts in some well-known encyclopaedias. Nevertheless I must say a few words on this large subject to explain some points about the early days of the Barber-Surgeons.

The origin of the whole Guild system is obscure and in some ways controversial, but there is no doubt that it was widespread in many parts of Europe long before it spread to our island.

The word " Gild " is of Saxon origin, originally meaning the payment of money or tribute, and it survives in the many Guildhalls of our cities and towns. I have seen a reference to a Merchants' Guild in Winchester in the reign of Ethelwulf, in A.D. 856. Merchants' Guilds (Gilda Mercatoria) undoubtedly arose in England before Craft Guilds or Fraternities, probably, as the Winchester record suggests, in the ninth century. Craft Guilds, including Barber-Surgeons, came later, and spread widely only after the Norman Conquest in the eleventh century. As Craft Guilds developed the older and fewer Merchants' Guilds gradually disappeared. Toulmin Smith, in his book, gives the original Ordinances of over 100 of the early English Craft Guilds ; and Charles Williams, surgeon and historian of the Norwich Guild of Barber-Surgeons, has provided some information of special interest for this Vicary Lecture, which is dealt with later.

What actually was a Gild or Guild? Samuel Johnson, in his famous Dictionary, gave quite a good definition, as follows: "A Society, Corporation, Fraternity or Company combined together by orders and laws made among themselves." He might have added that the Guilds all had a deeply religious origin (an alternative name for the Barber-Surgeons was the Guild of St. Magdalene) and that much of their activity, as it is to-day in the City Livery Companies, was devoted to the care of their poorer brethren. A Craft Guild bore no resemblance to a modern trade union, although in fact it was a local "closed shop." It had some slight resemblance to a modern friendly society; but really was quite different from either of these modern devices. Masters and men (i.e., the apprentices) were bound together by strict rules for the mutual benefit of each, and there was always a long period of apprenticeship—generally seven years—followed by a strict examination before admission, with subsequent entry as a Freeman on the local Roll. The Examiners or "Searchers," with a special badge of office referred to subsequently, included among their duties discipline among the apprentices, exclusion of poaching strangers, prevention of Sunday trading and all matters guarding the local monopoly of the Guild. Craft Guilds continued to flourish from the twelfth to the sixteenth century, but in the seventeenth century they went gradually into decline, and before 1750 most of them had ceased to exist. This was long before their powers were *officially* ended, and all Guild restrictions on trade abolished, by the Municipal Reform Act of 1839.

The origin of the Barber-Surgeons

There has been much speculation, and many hypotheses have been put forward to explain the association of Barbers and Surgeons, a union which at the time of its origin, however, was probably not nearly so curious and odd as it appears to us now. The union was certainly effective long before Craft Guilds crossed from the Continent to Britain, and the early story may for ever remain a Guild mystery.

To-day, I will only advance one well-known but simple hypothesis, having warned you that there are many others. In the early part of the so-called dark ages, monks in their religious houses were undoubtedly the first to attain to any primitive knowledge of the cure of diseases and the treatment of wounds and accidents. The monks had servants who among other duties were their barbers and shaved their tonsures. It is said that monks, by Papal Edict, were forbidden to shed blood, and passed on their knowledge of primitive surgery and of bleeding to their barber servants, who became in time recognised as Barber-Surgeons and founders of a Guild.

I have already noted that the Craft Guilds, including Barber-Surgeons, first spread widely over England soon after the Norman Conquest in 1066. The earliest mention of a Barber which I have been able to trace is from the Roll of Norwich Freemen, quoted by Charles Williams—John Belton, Barber, 1163. The word surgeon only appears later, and again my first

record is from Norwich—Randulph de Morlee, " Surgyon," 1288. Soon afterwards the names of Barber-Surgeons became quite numerous in many Freemans Rolls, and later still Leeches (Leches) and Apothecaries began to indicate their profession.

Fig. 3. Insignia of the early Company (not incorporated) of Surgeons in London.

It is of interest to note here that our first record for the parent London Company is of Richard le Barber, sworn in at Guildhall in 1308. Everything earlier, and there must have been much earlier records in London, is lost.

At first the art of Barbery and the primitive art of Surgery were no doubt easily combined in one person, the surgery being confined mainly to tooth-drawing and the treatment of minor wounds. Gradually, but quite early in the history of our Guild, some men restricted their practice to Barbery and others to Surgery (Fig. 3), and this dichotomy persisted uneasily during the hundreds of years in which Barbers and Surgeons were united in one Guild.

Most of the Guilds of Barber-Surgeons were small and simply concerned to maintain the local monopoly of their craft. Only a few of them possessed a Hall or meeting place of their own, but it was in some of these Halls, as will be seen, that the real foundations of Surgery began, with the provision of a dissecting room for the study of Anatomy.

Some Companies and Guilds of Barber-Surgeons

Clearly, for this lecture, I must select Companies and Guilds which have some special interest, and leave out historical details of many others for some possible future occasion. England, much the most populous and settled part of Britain in the years after the Norman Conquest, naturally had the greatest number of Guilds. Ireland, in the thirteenth century severely under the control of the Anglo-Norman dynasty, had a few very interesting companies of Barber-Surgeons, founded as will be seen later chiefly on the model of the Bristol Craft Guilds. Scotland, on the other hand, at that time and for much later struggling for independence, had few separate Craft Guilds, although I shall be speaking later about the Edinburgh Guild of Barber-Surgeons. In Scotland the control of trade developed slowly and rather differently, and even the early history of surgery was different, for instance, in Glasgow.

Wales, rather to my astonishment and disappointment, seems to be very destitute of Guild history, and the keeper of printed books in the National Library of Wales states that although Barbers, Surgeons and Apothecaries are mentioned in town records there is nothing to indicate that they ever formed themselves into a Guild. Perhaps the important city and port of Bristol, in which Guilds appeared so early, was too near.

In my description, pride of place must naturally go to the only two Companies or Guilds of Barber-Surgeons which, apart from our Livery Company in London, still remain in being. I shall then pass on to others of special historical interest, but all of which have long since expired.

Newcastle-upon-Tyne

I have very full information about the Newcastle Company, both from written sources and from friends. The Company has been fortunate in its historians, both past and present. The most complete account of it was given by the late Dr. D. Embleton, one of the early physicians of the Royal Victoria Infirmary, in a long booklet published locally in 1891, and in an article published in 1892. Various local Surgeons, especially the late Mr. Gray Turner, have shown great interest in the Guild. Mr. Hodgson and Emeritus Professor F. C. Pybus, both personally known to many senior Fellows of this College, are still interested, although neither of them is apparently eligible to become a member of the Guild. Professor Pybus published, in 1929, a long account of the Newcastle Barber-Surgeons, and this article, with some personal letters, has been of great help to me. Finally I have enjoyed discussions with Mr. L. C. Ramsay, the present Chief Steward (or Master) of the Company, who came as our guest to the Livery Dinner of the London Company in 1957, while I was Master.

The Incorporated Company of Barber-Surgeons, Wax and Tallow Chandlers of Newcastle-upon-Tyne, was founded on 10th October 1442, rather late in comparison with similar Guilds elsewhere. It was a local Craft Guild, and never had a Royal Charter. The oldest Minute book is lost, so that the earliest written records are included in a book which

covers the years 1616 to 1686. The Company was never large numerically. In 1616 there were sixty brethren ; to-day (in 1958) there are only seventeen ; and admission being solely by patrimony, in spite of various suggestions to change this rule, the continued life of the Company is obviously in peril. Not a single medical man, Barber, Wax and Tallow Chandler, remains. The Company meets once a year, on Trinity Monday, the day fixed for their chief meeting day and feast at their foundation in 1442 ; but feasts are now a thing of the past.

Our chief interest in the Newcastle Company must be in the history of their various meeting places or Halls, in which Anatomy and Surgery were actively taught for many years ; and in the relations of Barber-Surgeons Hall to the embryonic stage of the flourishing Medical School, which now forms the Faculty of Medicine of the University of Durham.

Their first meeting place was in a tower over one of the gates of the walled city—Pandon Gate. Plague in 1636 and war in 1644, when the city was beleaguered, ended this plan, for the tower was demolished to improve the defences. A house was temporarily rented in 1648, but at the same time the Company petitioned the Mayor and Corporation for a site on which to build a permanent Hall. A lease of land for sixty-one years at 6s. 8d. per annum was granted, and the Company also obtained additional adjacent ground to make a physic garden of medicinal herbs. The first Hall was occupied in 1652, and is the one so well described by Miss Celia Fiennes in the well-known Diary of her travels through parts of England on horseback in the reign of William and Mary (1689-1694). This intrepid lady, of the family still represented by the present Lord Saye and Sele, gives the most complete account now available of Barber-Surgeons Hall, its pretty herb garden and its Anatomy room with two bodies that had been anatomised. I have heard much about this lady and her Diary from one of the Fiennes family, recently Master of the Vintners' Company of London.

Dr. Embleton also gives a graphic account of the Company's main activities in their first Hall. As a charity they aided not only their own poor brethren, but also many other poor strangers and wanderers—maimed soldiers, ship-wrecked sailors and the like. They also made an annual grant to the Northumberland Plate, a famous horse race once run on the Town Moor but now nearby at Gosforth, and still known affectionately as the Pitman's Derby. There are full details of the teaching of Anatomy and Surgery, of the bodies of felons they obtained for dissection, of the books and skeletons they bought, and of the fine case of surgical instruments which they lent out to members of the Guild. There is reference to the "Searchers," who disciplined and examined the apprentices and dealt with quacks and poachers not belonging to the Guild. In 1711, as the fashion came in, Periwig making was added to their other activities.

Barber-Surgeons Hall was rebuilt on the same site in 1730, but in a different and more ornate style (Fig. 4). It was again surrounded by a

garden, in which some fine statues were erected. Professor Pybus has tried hard to discover the fate of these statues, but without success.

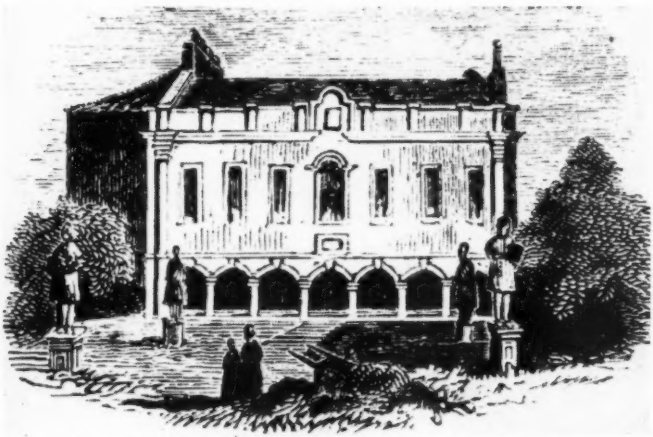


Fig. 4. Hall of the Barber-Surgeons of Newcastle-upon-Tyne. (This represents their Second Hall.)

The Company continued to meet in their new Hall until about 1830, but by this year their activities were obviously in acute decline, and the Hall stood empty for four years. It was at this time, in 1834, that the Hall was taken over by the newly formed Medical School of Newcastle, and active teaching was carried on until 1851. At that date the railway company obtained powers to extend the Central Station and demolish the Hall, but this was conditional to a new third Hall being built, in which the Medical School continued its teaching until 1857. About that period there was an unfortunate split in the Medical School, and the minority group retained possession of Barber-Surgeons Hall. Peace was restored, the Hall became redundant, and was finally sold to the Parish of St. Paul as a school, which it still remains.

The Coat of Arms of the Newcastle Company (Fig. 5) is unusual in showing clearly the union of Barber-Surgeons with Wax and Tallow Chandlers. There are two shields, that on the left practically identical with that of the London parent Company of Barber-Surgeons, that on the right presumably representing the Chandlers.

How has this old Company in Newcastle managed to survive? The main reason would appear to be the continued activity of the Freemen of the City for the preservation of the Town Moor, a very large open space of great value belonging to the citizens. Many threats to build on the moor or to spoil it in other ways have been thwarted by the watchfulness of the Freemen, the survivors and representatives of the ancient Guilds.

Fig. 5. Coat of Arms of the Barber-Surgeons, Wax and Tallow Chandlers, of Newcastle-upon-Tyne.

The Company of Barber-Surgeons, Wax and Tallow Chandlers, of Chester

It was only quite recently that I discovered that this Company or Guild still survives in Chester, and I am greatly indebted to Miss E. Finch, City Archivist, for putting me on the right track to obtain all the information which I so far possess. Miss Finch kindly sent me a long article, of over 100 pages, said to have been delivered to an Archaeological Society in 1911 by Mr. Frank Simpson. This article or lecture deals with all the Guilds of Chester, but with special emphasis on the Barber-Surgeons. Miss Finch also put me in touch with Dr. C. K. Sconce of Chester, who had lectured on the Barber-Surgeons when President of the Chester and North Wales Medical Society, but his lecture was never printed. Miss Finch was also able to provide the name of the present Chief Steward of the Chester Guild, Mr. R. F. M. Roberts, and to obtain some important details from him on my behalf.

It is clear from what Mr. Frank Simpson states, that he had full access in 1911 to the records of the Guild, which were placed at his disposal by Mr. R. Roberts, at that time said to be the sole surviving member

of the Company. Now, Miss Finch informs me after her inquiries from the present Chief Steward, Mr. R. F. M. Roberts, the brethren are six in number. One is over eighty years of age, but there are three prospective entrants, sons of present members, who will probably be admitted within two years. A meeting takes place once a year at the home of the Chief Steward, who is understood to have all records of the Guild in his possession.

The Chester Guild of Barber-Surgeons is clearly, from Mr. Simpson's account, a very old foundation, probably dating from the early fourteenth century. The Miracle plays, in which all the City Guilds took part, were first performed in Chester in 1328, and the Barber-Surgeons are then recorded as having acted Abraham and Isaac or the Slaughter of the Innocents. It is also on record, this time in the city archives, that in 1376 there were twenty-six Guilds or Companies in Chester, and the Barber-Surgeons, as in other places united with the Wax and Tallow Chandlers, ranked third on the list.

Four Minute books are said to exist, the first beginning in 1606. In 1698, when the second book commences, the Company consisted of one Alderman, one Chief Steward, and forty-one brethren. The fourth volume, begun in 1842, is believed to be still in use. All the original local charters of this Guild, issued by the City Mayor and Common Council, are lost; but copies of two of them, dated 1540 and 1550, are included in the second Minute book. The Guild never had a real Hall, and was never concerned with the teaching of Anatomy or Surgery. It met for many years in a tower on the city walls, the Golden Phoenix or King Charles' Tower. This was much damaged during the siege of Chester by the Parliamentarians in 1645 to 1646, but was rebuilt and again used by the Barber-Surgeons. It was too small for feasts, and the meetings adjourned to various inns in the city.

Why did this small local Guild not die out, as in so many other cities, and why is it alive to-day? The reason is a fascinating one, and is concerned with the Owen Jones bequest. I can here only deal briefly with the matter and full details are given by Frank Simpson. Owen Jones, a resident of Chester, by his will dated 14th February 1658, bequested his small landed estate in the County of Denbigh for the benefit of the poor of the Gilds and Companies of Chester. In 1743 the income from the estate was £16 17s. 4d., which gradually increased to £40. Then suddenly a rich seam of lead was found on the land, the mining rights were leased to a company for thirty-one years in 1758, and the financial results were marvellous. For instance, it is on record that in January 1792 one small Guild, the Barber-Surgeons, after paying all expenses, distributed the sum of £391 16s. 0d. among its twenty-six brethren. Various portions of the land were sold in 1864 for £22,092, but a rental value of £116 still remained; and in 1870 Royalties for the mineral rights still amounted to £1,840 for the year. It is not surprising that in 1892 the Charity Commissioners were called in, since so much money was being distributed

among so few persons. They drew up a scheme, still in being, which among other benefits to the city of Chester provides free education and many other advantages to young citizens of Chester, particularly if their parent is associated with one of the old Guilds. It is perhaps not surprising that the few remaining Barber-Surgeons of Chester are a little reticent about their doings, and still hold their papers and records firmly in possession.

The Seal of the Company has been lost, but apparently they used, as did other similar Guilds, the Coat of Arms of the London Company.

The Barber-Surgeons, Wax and Tallow Chandlers, of Norwich

The Barber-Surgeons of Norwich are fortunate in having had a splendid local historian, Mr. Charles Williams, F.R.C.S., Surgeon to the Norfolk and Norwich Hospital at the turn of the present century. Through the kindness of Mr. Blaxland, Surgeon in Norwich, who remembers Mr. Williams well, I was put in touch with the son of Mr. Williams, who kindly loaned me some of his father's papers to which (with other publications) reference is made.

The Barber-Surgeons of Norwich was founded as a Company long before 1388, but its earliest records are lost. In 1388, however, an interesting historical event occurred which, as will be seen, is of great interest for the history of *all* Barber-Surgeons. In that year Richard II sent out writs throughout his Kingdom to enquire into the nature and constitution of the Guilds. The replies were all, or nearly all, stored in the Tower of London, but were in some unknown way destroyed. By good fortune the replies of Norwich and Lincoln went elsewhere, and are still preserved in the Public Records Office. The Norwich reply provided Williams with a fund of interesting information, of which he took full advantage. He gives the full reply to the King, changed into modern English, which is well worth reading. Like all Guilds, when asked their age, the Norwich Guild replied that they went back " whereunto the memory of man knoweth not." As in other places the Barber-Surgeons of Norwich appear to have been united from their foundation with the Wax and Tallow Chandlers.

The reply also gives important information, not available elsewhere, of the number of Craft Guilds not only in the city of Norwich—thirty-seven in all—but also in the County of Norfolk—909 in all. This is the best evidence we possess of the number of Guilds which must have existed all over England at that time.

The Norwich Guild was simply a local Craft Guild, under the control of the Municipality. It had no Hall, but met, like other Guilds, in the city Guildhall. No Minute books remain, but Williams found many references to the Guild in the Assembly Rolls and Freemans Rolls of the city, some of which have already been mentioned in this lecture.

In 1684 a new formal set of Ordinances was drawn up, and is preserved in the Muniment Room of the Castle Museum at Norwich. The last

official reference to the Barber-Surgeons of Norwich is in the Assembly Roll for 1723, and the Guild presumably came to an end soon afterwards.

The Barber-Surgeons of York (Ebor)

The Barber-Surgeons of York (Ebor) were also fortunate in having a good local medical historian, Dr. G. A. Auden, father of the famous poet, and to his paper I am chiefly indebted. The Guild in York was obviously very ancient, and in the roll of Freemen of the city, which begins in 1272, the first Barber (Rogerus le Barber) was noted as admitted in 1290. This is eighteen years in advance of the first recorded Barber of the London Company.

An early entry about Barber-Surgeons in the Exchequer accounts of York for 1346 is of much interest. It records " Payments to William de Bolton and Hugo de Kilvington, Barber-Surgeons, going from York to the Castle of Bamburgh (in Northumberland) to heal the said David de Brus who lay there, having been wounded with an arrow at the said battle, and to extract the arrow and to heal him with despatch . . . £6." The battle referred to is Nevilles Cross, fought in 1346, and David de Brus was the younger brother of Robert the Bruce, King of Scotland, and victor of Bannockburn. The two Barber-Surgeons must have made a good job of it for David de Brus, after being ransomed, became King David of Scotland and lived for long afterwards.

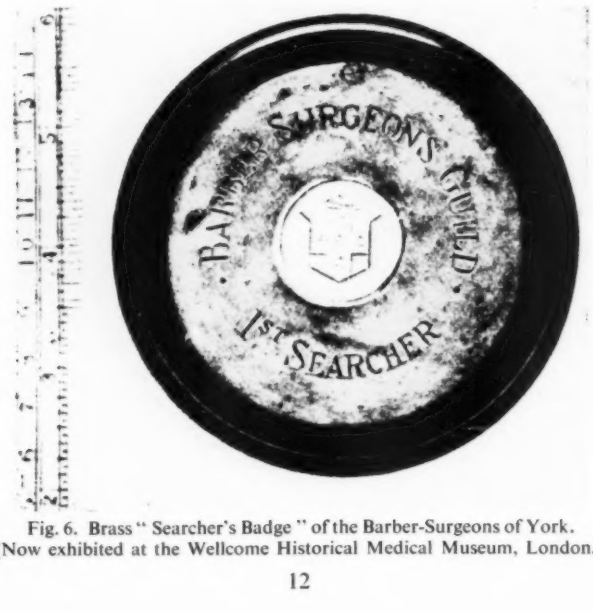


Fig. 6. Brass " Searcher's Badge " of the Barber-Surgeons of York.
(Now exhibited at the Wellcome Historical Medical Museum, London.)

The Ordinances and Rules of the Company certainly date far back in history, and in 1486 was begun their famous illustrated Book of Ordinances, purchased and now carefully preserved by the British Museum (Egerton MSS. 2572). This lovely book, which I have myself examined, contains paintings of the Coat of Arms of the Barber-Surgeons (identical with those of London) and also of Henry VII, Henry VIII, Edward VI, Mary, Elizabeth, James I and Charles I. In the Ordinances there is a full account of the " Searchers " who had many duties, including the discipline and examination of the apprentices and the seeking out and reporting to the Municipality of poachers coming unlawfully into the city to practice their craft. Searchers had a brass arm-badge of office, and the only one known to exist belonged to the Barber-Surgeons of York and is now exhibited at the Wellcome Historical Museum (Fig. 6).

Apart from their famous Book of Ordinances, no written records of the Company have yet been found, and it is believed to have dissolved about 1721 or shortly afterwards.

I am much indebted to Revd. Angelo Raine and Mr. Bernard P. Johnson, both of York, for help, as well as to Dr. Auden.

The Barber-Surgeons of Bristol

I am disappointed that I have been able to obtain so little information about the Barber-Surgeons of Bristol, which must have been one of the earliest and most important Guilds of its kind outside of London. This will be evident when I am dealing with Barber-Surgeons in Ireland, for in the early days Bristol was the chief English port trading with Ireland and Bristol was the model for many trade and craft usages in Ireland. Moreover, Bristol was the home port of famous merchant adventurers, Cabot and others, whose ships required surgeons provided locally, as surgeons were provided and examined for so many years by the London Company for the Navy. Much of my information so far about Bristol has been obtained from a paper by George Parker, M.D., Physician to the Bristol General Hospital, who in 1912 wrote on Barber-Surgeons in general. This contained much valuable and curious information which I have used elsewhere, but unfortunately too little reference to Bristol itself.

In *The Little Red Book of Bristol*, a treasure not allowed out of their City Library, three copies of Ordinances of the Barber-Surgeons are given, the first dated September 1395, the second 1408, and the third, an extension of the first two, in 1439. The third Ordinances were fully confirmed by the Mayor and Sheriff of Bristol in the same year, after which there comes a long gap until 1652. At this time the Common Council of the city confirmed the ancient rights of the " Barbers and Chirurgeons " and made some important new rules for the Company. One of these enjoined that " every Surgeon entering for a voyage as Surgeon of a ship of the port shall have his chest (i.e. of instruments) examined by the Master and two others, that it be well furnished with all things necessary for the said voyage."

Parker, by persistent enquiry under considerable difficulties, established that the Barber-Surgeons of Bristol had a Hall of their own, and moreover that it still existed in a dismantled condition in 1911 as part of the Bunch of Grapes Inn and Restaurant in Exchange Avenue (Fig. 7). From his inspection he felt sure that the Hall originally contained a theatre for Anatomy, but written evidence is absent.

Fig. 7. Barber-Surgeons' Hall, Bristol.
(All that remained of it in 1911 (Parker.))

The usual quarrels and differences between Barbers and Surgeons occurred in Bristol, and in 1739 the Barbers made a plea to the Common Council with "complaint of their grievances and ill treatment by the Surgeons." This availed nothing, for the Surgeons quickly seceded; and the Barber-Surgeons apparently came to an end about 1742, when their Hall was sold as a coffee house.

An interesting point, stated by Parker, but without detailed evidence, is that in 1912, when he wrote his paper "a single member of the Company recently remained." One wonders if this single member possessed any documents or other treasures which may still come to light in Bristol !

The Barber-Surgeons in Ireland

Dublin

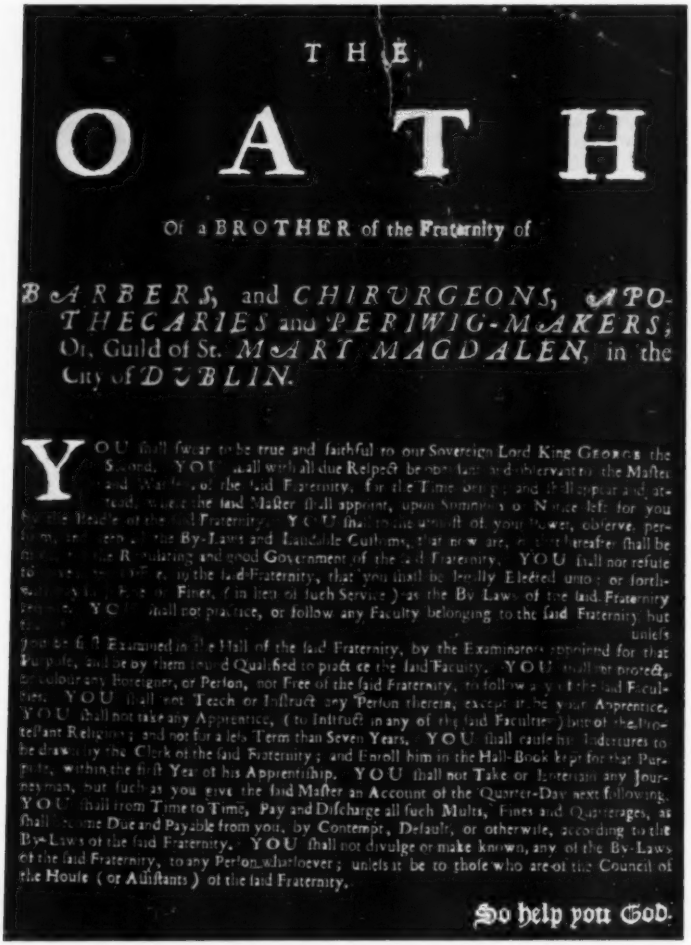
Pride of place must naturally go to Dublin, although to amplify the scanty history of Guilds in Dublin, in the early days, I have had to fall back to some extent on the written history of Limerick ! In a history of Limerick it is stated that in 1192 Prince John, who had been declared King of Ireland in 1177 and was later to be crowned King John of England in 1199, granted a Charter to Dublin to form Craft Guilds like those of Bristol. In 1199 he granted the same privileges by Charter to Limerick, and possibly also to Cork. A long gap exists in Dublin history until 18th October 1446 when, in the reign of Henry VI of England, a Royal Charter was granted to the " Guild of St. Mary Magdalene of the City of Dublin." A second Royal Charter was obtained in 1577, in the reign of Elizabeth, which definitely gave the Guild of St. Magdalene jurisdiction over all those who " carried on the calling of Apothecaries, Surgeons or Barbers in Dublin." Thus, different from London, the Apothecaries in Dublin were united with the Barber-Surgeons. The Royal Charter of Henry VI (1446) is claimed to be the first Royal Charter awarded to any Company of Barber-Surgeons ; and even in this old Charter the troubles of Ireland are apparent, for it is enacted that all the members must be English born.

Just as in London the union of Barbers and Surgeons was not always cordial, and it is clear from the wording of the Charter of Queen Elizabeth that a final attempt was being made to bind the Surgeons and Barbers firmly in one Guild.

A third Royal Charter in 1687 (James II) also firmly incorporated the Apothecaries and Peruke-makers with the Barber-Surgeons (Fig. 8). At this time the combined Guild had a Hall of their own in Smock Alley, and an account of one of their meetings there (Thomas Collins, Master) on the 28th February 1714 survives.

The Apothecaries gradually became the richest section of the Incorporated Guild, for they made money on all drugs coming into Ireland. In 1745, in the reign of George II, they obtained a new Royal Charter separating themselves completely from the Barbers, Peruke-makers and Surgeons. This Charter contained, as for all the city Guilds of Dublin at that time, provision against the admission of Roman Catholics—a continued source of trouble. In 1789 the Apothecaries applied to Parliament for permission to establish an Apothecaries' Hall, similar to that in London. Permission was granted in 1791, and within a year their new Hall in Mary Street was built and occupied. The Apothecaries' Hall of

Dublin still exists as a Licencing Body to-day but has changed its site Meantime, as in London, the Surgeons had again been restive and had formed a separate society without a Charter. In 1784 the Surgeons finally obtained the first Charter of the Royal College of Surgeons of Ireland, nearly forty years after the separation of Barbers and Surgeons in London. Thereupon the Barber-Surgeons Company fell quietly into decline and



THE

OATH

Of a BROTHER of the Fraternity of

BARBERS, and *CHIRURGEONS*, *APOTHECARIES* and *PERIWIG-MAKERS*; Or, Guild of St. *MARY MAGDALEN*, in the City of *DUBLIN*.

YOU shall swear to be true and faithful to our Sovereign Lord King GEORGE the Second. YOU shall with all due Respect be obedient and observant to the Master and Wardens of the said Fraternity, for the Time being; and shall appear, at ready, when the said Master shall appoint, upon Summons or Notice left for you at the Dwelling-House of the said Fraternity. YOU shall to the utmost of your Power, observe, perform, and keep all the By-Laws and Laudable Customs, that now are, or shall hereafter shall be made for the Regulating and good Government of the said Fraternity. YOU shall not refuse to [illegible] to the said Fraternity, that you shall be legally Elected unto or forthwith pay the Fines, (in lieu of such Service) as the By-Laws of the said Fraternity appoint. YOU shall not practice, or follow any Faculty belonging to the said Fraternity, but [illegible] unless you be first Examined in the Hall of the said Fraternity, by the Examinators appointed for that Purpose, and be by them found Qualified to practice the said Faculty. YOU shall not protect, or colour any Foreigner, or Person, not Free of the said Fraternity, to follow any of the said Faculties. YOU shall not Teach or Instruct any Person therein, except it be your Apprentice. YOU shall not take any Apprentice, (to Instruct in any of the said Faculties) but of the Protestant Religion; and not for a less Term than Seven Years. YOU shall cause his Indentures to be drawn by the Clerk of the said Fraternity; and Enroll him in the Hall-Book kept for that Purpose, within the first Year of his Apprenticeship. YOU shall not Take or Entertain any Journeyman, but such as you give the said Master an Account of the Quarter-Day next following. YOU shall from Time to Time, Pay and Discharge all such Mulcts, Fines and Quarterages, as shall become Due and Payable from you, by Contempt, Default, or otherwise, according to the By-Laws of the said Fraternity. YOU shall not divulge or make known, any of the By-Laws of the said Fraternity, to any Person whatsoever; unless it be to those who are of the Council of the House (or Assistants) of the said Fraternity.

So help you God.

Fig. 8. Oath of a Brother of the Barber-Surgeons of Dublin.
(In Trinity College Library, Dublin.)

finally expired. All their existing records have, however, been deposited in a chest in the Library of Trinity College, Dublin, where I have been able to examine them. The original Charter of Henry VI is lost, but those of Elizabeth and James II remain. The list of brethren finally closes in 1840, and it is believed that all the papers were deposited at Trinity College by William L. Moore, author of *An Outline of the History of Pharmacy in Dublin*, published in Dublin in 1848.

At their commencement in 1446 the Barber-Surgeons of Dublin used the same Arms and Seal as the London Company, but in 1645 they received a grant of Arms of their own, and I am able to show you an impression of their Seal (Fig. 9).

Fig. 9. Drawing of wax impression of the ancient Seal of the Barber-Surgeons of Dublin.
(Note the crowned harps, and other differences from the Arms of the London Company. Drawn by Miss Helen Wilson, F.I.A.L. Seal in Trinity College Library, Dublin.)

Limerick and *Cork* both had Guilds of Barber-Surgeons. In Cork no records or papers have survived, and the first mention of the Guild in

the City records is as late as 1656. Limerick fortunately possessed a good local historian in Robert Herbert, whose paper on the Trade Guilds of Limerick, published in 1941, contains not only valuable information about the local Barber-Surgeons but about similar Guilds elsewhere. As has been stated earlier Prince John, later King John of England, granted the first Charter to the Guilds of Limerick in 1199, and a second Charter was granted by Edward I in 1291, Bristol being quoted in both instances as the example to follow. All native Irish were excluded from the Guilds, a source of much subsequent trouble. In 1769 fifteen Guilds existed in Limerick, including separate Guilds of Surgeon-Barbers and of Tallow Chandlers. By 1833 the " Commissioners on Municipal Corporations in Ireland " found twenty-one Guilds still existing in Limerick, but the Surgeon-Barbers had already ended before the others were made to follow suit. The Limerick Guild is said to have used the same Seal as that granted to Dublin in 1645, and in 1874 their Seal is said to have been exhibited to the Royal Society of Antiquarians of Ireland, but its present whereabouts is unknown.

The Barber-Surgeons in Scotland

Up to 1018, according to Comrie, the counties which now form South East Scotland were part of the Anglian Kingdom of Northumbria, and the town of Berwick was included in this area. In 1249 Berwick, although by then included in Scotland and its principal early port, is said by Cochran-Patrick to have established Guild laws (Statuta Gilde) and to have had a Dean of Guild. This may be the first impact of Guilds in Scotland, but the Guild system evidently did not spread in the same way in Scotland as in the south, although Trades Houses and Deans of Guild exist in the cities even to-day.

Edinburgh

The only important Guild of Barber-Surgeons in Scotland was in Edinburgh, and was incorporated by a Charter of the Town Council, termed a Seal of Cause, on 1st July 1505. This Charter was ratified by James IV in 1506, and again by James VI in 1613 (Struthers, Scott Moncrieff, Wade). By the Charter one body was allowed annually for dissection.

As occurred elsewhere the Surgeons gradually began to consider themselves superior to the Barbers and to drift apart. The first step towards separation came in 1648 when, according to the Barbers, there were ten surgeons practising in Edinburgh and only six Barbers. In the following year Barbers were excluded from the Guild unless they could pass an examination in Surgery, and according to Scott Moncrieff practising Barbers became hard to find in Edinburgh. Difficulties continued and in 1694 the Surgeons really separated from the Barbers but took in the Apothecaries, thus creating a new mongrel calling—a Surgeon-Apothecary. This aroused the Barbers, who raised a Court action in 1718 to restore

their ancient rights, granted in 1505. The Surgeons lost their case, but things went on as before, although the Apothecaries now came under the wing of the College of Physicians of Edinburgh, founded in 1681.

From 1718 the separation of Barbers and Surgeons in Edinburgh was for practical purposes complete, but the final formal separation only came in 1845, when the Surgeons obtained from Parliament a new Grant of Incorporation by which they were relieved of all obligations to the Barbers in consideration of an annual payment of £10. This was the death knell of the Barber-Surgeons Guild, the last meeting of which was held in September, 1892, with two members present, father and son.

ACKNOWLEDGMENTS

Personal friends, city archivists, librarians, and others to whom I have written for local information, have all helped greatly in providing the material for this Vicary Lecture. They are too many to mention individually, and I wish now to thank all of them sincerely for their interest and courtesy.

REFERENCES

AUDEN, G. A. (1928) The Gild of Barber-Surgeons of the City of York. *Proc. Roy. Soc. Med.* **21,** 1400.

COCHRAN-PATRICK, R. W. (1892) *Mediaeval Scotland.* Glasgow, James Maclehose.

COMRIE, J. D. (1932) *History of Scottish Medicine.* 2nd edition, 2 volumes. London, Bailliere, Tindall, and Cox.

DOOLIN, W. (1951) Dublin's Surgeon-Anatomists. *Ann. Roy. Coll. Surg. Engl.* **8,** 1.

EMBLETON, D. (1891) *Barber-Surgeons and Chandlers of Newcastle.* Newcastle-upon-Tyne, Daily Journal Office. 84 pages.

———— (1892) The Barber-Surgeons and Tallow Chandlers of Newcastle-upon-Tyne. *Archaeologia Aeliana* **15,** 228-269.

FIENNES, CELIA (1888) *Through England on a Side-saddle in the time of William and Mary; being the Diary of Celia Fiennes.* London, Field and Tuer.

———— (1949) *Journeys,* edited with notes by C. Morris. Foreword by G. M. Trevelyan. New, revised edition. London, Crosset Press.

FLEETWOOD, J. (1951) *History of Medicine in Ireland.* Dublin, Browne and Nolan.

GROOMBRIDGE, M. J. (1952) The City Gilds of Chester. *J. Chester Archaeolog. Soc.,* new series **39,** 1.

HERBERT, R. (1941) The Trade Guilds of Limerick. *North Munster Antiquarian Journal* **2,** no. 3, 121 & 132.

KEEVIL, J. J. (1957) *Medicine and the Navy,* Vol. I. Edinburgh, E. & S. Livingstone.

LAMBERT, J. M. (1891) *Two Thousand Years of Gild Life.* Hull, A. Brown ; London, Simpson.

MCWALTER, J. C. (1916) *A History of the Worshipful Company of Apothecaries of the City of Dublin.* Dublin, E. Ponsonby, 166 pages.

MONCRIEFF, R. S. (1912) Note on the Incorporation of Surgeons and Barbers. *Edin. med. J.,* new series **9,** 524.

MOORE, W. D. (1848) An outline of the history of pharmacy in Dublin. *Dublin Quart. J. med. Sci.* **6,** 64.

O'SULLIVAN (1937) *Economic History of Cork.* Cork, University Press. References to Guilds, including Barber-Surgeons.

PARKER, G. (1911) Medical organisation and the growth of the medical sciences in the seventeenth century. *Bristol med. chir. J.* **29,** 201.

———— (1912) The Barber-Surgeons. *Bristol med. Chir. J.* **30,** 327.

———— (1922) Early Bristol medical institutions, the mediaeval Hospitals, and Barber-Surgeons. *Trans. Bristol and Gloucestershire Archaeol. Soc.* **44,** 155-178.

PYBUS, F. C. (1929) The Company of Barber-Surgeons and Tallow Chandlers of Newcastle-upon-Tyne. *Newcastle med. J.* **9,** 147 and *Proc. Roy. Soc. Med.* **22,** 287 (Read 17 Dec., 1924).

SIMPSON, F. (1911) The City Guilds or Companies of Chester, with special reference to that of the Barber-Surgeons. *J. Chester Archaeol. Soc.* n.s. **18,** 98-203.

SOUTH, J. F. (1886) *Memorials of the craft of surgery in England.* London, Cassell.
STRUTHERS, J. (1867) *The Edinburgh Anatomical School.* Edinburgh, Maclachlan and Stewart.
TOULMIN SMITH, J. (1881) *English Gilds.* London. Early English Text Society.
WADE, H. (1949) The Barber-Surgeons of Edinburgh. *Ann. Roy. Coll. Surg. Engl.* **5**, 53.
WALKER, J. and RICHARDSON, M. A. (1824) *The armorial bearings of the several incorporated Companies of Newcastle-upon-Tyne.* Newcastle, Edward Walker. 64 pages.
WALL, C. (1937) *The History of the Surgeons Company*, 1745-1800. The Thomas Vicary Lecture for 1935, expanded. London, Hutchinson.
WIDDESS, J. D. H. (1949) *An account of the Schools of Surgery, Royal College of Surgeons, Dublin*, 1789-1948. Edinburgh, E. & S. Livingstone.
WILLIAMS, C. (1896) *The Barber-Surgeons of Norwich.* Norwich, Yarmouth, and London ; Jarrold. 31 pages.
———— (1900) The Ordinances of the Gild of Barber-Surgeons of Norwich. *The Antiquary*, n.s., no. 129.
The Ancient Ordinary of the Barbers and Surgeons of York, A.D. 1486 *; with the new Ordinances of A.D.* 1592 *and* 1614. British Museum, Egerton MSS. 2572.
Documents and Seal of the Barber-Surgeons of Dublin, in Trinity College Library, Dublin.

PROCEEDINGS OF THE COUNCIL IN DECEMBER

AT A MEETING of the Council on 11th December, with Professor Sir James Paterson Ross, President, in the Chair, Lord Cohen of Birkenhead was appointed the first Watson-Jones Lecturer.

Mr. A. Dickson Wright was appointed Bradshaw Lecturer for 1959.

The appointment of Professor R. V. Bradlaw as Menzies Campbell Lecturer was announced.

A Moynihan Lectureship was awarded to Professor Englebert Dunphy of Harvard Medical School.

An endowment of £150,000 for the Chair of Pharmacology from Mr. G. A. Vandervell was most gratefully accepted.

The Begley Prize was presented to Mary Elizabeth Ashworth, of Charing Cross Hospital Medical School.

Diplomas of Fellowship were granted to 100 candidates, named in the list on page 64.

The following hospitals were recognised under paragraph 23 of the Fellowship Regulations :

HOSPITALS	POSTS RECOGNISED		
	General (all 6 mths.)	Casualty (all 6 mths.)	Unspecified (all 6 mths.)
COVENTRY—Coventry and Warwickshire Hospital (Additional)		J.H.M.O. (Cas. Off.)	
RICHMOND, Surrey — Royal Hospital (Additional)	Regr. (R.S.O.) S.H.O.	S.H.O. (Cas. & Orth.)	
EPPING—St. Margaret's Hospital (Additional)	H.S.		
LONDON — Prince of Wales's General Hospital (Additional)		S.H.O.	
ILFORD—King George Hospital (Additional)			Regr.

PROSTATIC OBSTRUCTION

Lecture delivered at the Royal College of Surgeons of England
on
17th April 1958
by
C. A. Wells, F.R.C.S.
Professor of Surgery, University of Liverpool

INTRODUCTION

THIS PAPER IS presented as a postgraduate lecture in which the subject under discussion is treated in a broad and comprehensive fashion. The views expressed are based upon twelve years of experience during which every case presenting primarily as prostatic obstruction has been treated along the lines hereafter indicated. The usual members of a clinical team have shared the operating and supervising of after-treatment. In benign, senile enlargement (apart from patients presenting in the course of pneumonia or cardiac failure) preliminary drainage has been rigidly excluded. Complete retention, with this exception, has been treated by emergency prostatectomy in every case, whether by day or by night.

Statistics are not presented and would be inappropriate in such a lecture but the overall impression is perfectly clear and strictly relevant. Mortality has shrunk to vanishing point and for practical purposes has not occurred from any of the hazards directly connected with the operation, such as haemorrhage, pyelonephritis, uraemia and renal failure. Cerebral haemorrhage, pulmonary embolism and coronary thrombosis have each been recorded. Deep vein thrombosis of the leg has been exceedingly rare. One patient only has developed post-operative urinary obstruction, attributable to an atypical stricture of which the origin remains obscure. No other patient has needed further treatment after the initial period of follow-up, during which a stitch and a stone have had to be removed from the bladder per urethram.

These results have been obtained in a general surgical clinic and can be reproduced elsewhere if the underlying principles are thoroughly grasped and the whole system of treatment applied with unremitting care and attention to detail.

Above all it must be remembered that the operation is not the treatment : it is one incident (albeit a very important one !) in the treatment which must be continued, step by step, until the bladder is free from obstruction and the urine free from infection.

PATHOLOGY

" Prostatic " obstruction occurs in the following conditions :

1. Benign senile enlargement.
2. Carcinoma.
3. Marion's disease.

4. The fibrous prostate.
5. The calculous prostate (? an entity).
6. The post-operative bar or diaphragm.
7. Urethral valves—seen only in early childhood and not discussed in this paper.

Benign senile enlargement

Aetiology. This condition arises in the later years of life presumably in response to varying hormonal influences. It is in many respects comparable with nodular enlargement of the thyroid, being compounded of hyperplasia, hypertrophy and interstitial fibrosis. As in the thyroid the change is irreversible, in contrast to the hypertrophy of the prostate which can be produced experimentally in dogs and reversed by reversing the hormonal processes.

Pathology. The enlarged portion of the gland occupies and follows the form of the lateral lobes and the median lobe. This diseased portion is conveniently known as the " adenoma " although it is not in the strict pathological sense a benign tumour. Like the nodular enlargement of the thyroid, to which it has already been compared, it can be enucleated from within a capsule of compressed normal gland. The whole of the " adenomatous " portion lies proximal to the verumontanum.

Carcinoma of the prostate

Aetiology. This tends to arise in a rather younger age group than that of the benign lesion although by no means necessarily so. There is no known aetiological factor.

Pathology. The growth may be found complicating a pre-existing " adenoma " or, very much more commonly, arising *de novo*. In the latter case the posterior lobe, i.e., the portion between and distal to the ejaculatory ducts, is commonly involved, which accounts for the palpable ridge in the midline obscuring the space between the lateral lobes.

The growth extends through the capsular tissues and may invade the base of the bladder or the peri-vesical tissues. Ulceration through to the rectum is extremely rare even when the mass has attained a very large size.

Secondary deposits arise chiefly in bone, and mostly in the pelvis and lower lumbar spine. Remote deposits to other organs, to bone, to skin or elsewhere, occur but rarely.

The bony deposits are osteoblastic rather than osteoclastic. In the presence of osteoblastic secondaries the serum acid phosphatase is usually considerably raised, e.g. to ten or more King Armstrong Units. Otherwise normal levels of two to three units are the rule, even in the presence of advanced prostatic carcinoma.

Marion's disease

This is a change at the neck of the bladder involving the neuro-muscular mechanism rather than the prostate itself. There is hypertrophy of the

internal sphincter and failure of this muscle to relax when the bladder contracts. The condition may arise in infancy, childhood or later in life. When patients present in the prostatic age group and are found to have Marion's disease there is invariably a long history.

When the condition has been present for many years it is probable that much of the muscle gets replaced by fibrous tissue. The secondary back pressure effects are particularly important in this condition.

Fibrous prostate

This is an important pathological entity. The prostate itself is very little, if any, larger than normal but it is unusually tough and by its configuration causes obstruction at the neck of the bladder. There is no " adenoma " and consequently no tissue plane for enucleation.

Calculous prostate

Prostatic calculi are particularly liable to be found in the small fibrous gland but may also occur in benign senile enlargement. This does not constitute an important pathological entity. The calculi are either within the substance of the prostate or lie between the " adenoma " and its pseudo-capsule. They are said to arise from corpora amylacea and are in no sense true urinary calculi.

On palpation the stones may be confused with carcinoma but they are always opaque to X-ray.

Post-operative bar or diaphragm

Obstruction at the bladder neck after operation may be due to the following causes :

(*a*) The formation of a diaphragm at the level of the internal sphincter especially after Freyer's operation, q.v.

(*b*) After the excision of a median wedge for the relief of Marion's disease owing to the falling together of the two sides of the wedge and the reconstitution thereby of a fibrous bladder neck.

(*c*) After a retropubic prostatectomy or any other procedure in which the pseudo-capsule of normal tissue is transgressed, or in which there is a haemorrhagic or inflammatory collection outside the capsule during the period of healing.

SECONDARY EFFECTS OF PROSTATIC OBSTRUCTION

Bladder

In response to obstruction, the muscle hypertrophies. The lining of the bladder may remain smooth or may show deep trabeculation. In between, the trabeculae saccules form and may ultimately develop into diverticula, consisting of little more than mucous membrane covered by a few scattered muscle fibres. Diverticulum formation is particularly liable to occur in Marion's disease where the back pressure continues for many years, in contrast to the shorter duration of prostatic enlargement.

The diverticulum in turn is likely to be complicated by the development in its depths of carcinoma. This is consistent with the concept that carcinogens, concentrated in the urine, are most likely to produce growths in those parts to which they are most continuously exposed. The diverticulum never empties and is therefore in contact with its content of urine all the time.

Atrophy after hypertrophy, leading to atonic dilatation, is a popular concept in the bladder as in other hollow organs subjected to obstruction. The fact is that the more a hollow viscus is distended the more difficult is it for the muscle in its wall to produce an effective contraction. Once the obstruction has been removed, however, the bladder rapidly regains its normal tone and persisting atony after operation is a notion which should be accepted only with great reluctance.

Ureters

Increasing distension of the bladder usually has the following effects upon the ureters :

1. Unfolding of the uretero-vesical valve which becomes incompetent.
2. Dilatation of the lower ureter and ultimately the whole ureter, and
3. Hydronephrosis of a mixed pelvic and renal type with, ultimately, tubular destruction.

Infection

It is a fair aphorism that infection does not occur—it is caused.

1. The urine is normally sterile and remains so unless infection is introduced. 85 per cent. of patients with prostatic obstruction who have not been subjected to instrumentation have sterile urine.

2. Acute pyelonephritis and cystitis may be blood borne in a patient suffering from prostatic obstruction, just as in any other, but this is a rare event. In such a case the existence of residual urine prevents the resolution of the infection which becomes chronic.

3. Instrumentation—the passage of a bougie, catheter or cystoscope always carries with it the risk of contamination. In the presence of residual urine contamination becomes established infection. This causes (*a*) cystitis, (*b*) pyelonephritis, if the ureters are dilated, and (*c*) epididymitis in a percentage of cases.

Azotaemia—uraemia—acidosis

The retention in the blood stream of waste products may be the result of any one of the following four causes :

1. *Obstruction alone.* The urinary tract remains undamaged but the urine does not get away and therefore the waste products accumulate.

2. *Obstruction with reversible hydronephrosis.* This is, pathologically, essentially the same as obstruction alone but the risk of renal damage is in sight.

3. *Obstruction with established hydronephrosis.* Here the hydronephrosis has resulted in destruction of renal substance and particularly loss of tubular function. The kidney is beginning to lose its power of concentration. Glomerular filtration remains unaffected for a longer time. Such kidneys can put out very large quantities of dilute urine with a specific gravity consistently round about 1,010.

4. *Pyelonephritis.* This infective complication usually arises as a sequel to instrumentation. It is unlikely to occur unless there is hydroureter and hydronephrosis but it probably can occur despite normal ureters in patients subjected to prolonged catheter drainage and kept lying flat in bed in which position gravity does not assist the drainage of the kidneys and the ureters.

TESTS OF RENAL FUNCTION

It is important to realise two basic facts :

1. The presence of prostatic obstruction and residual urine make it impossible to carry out any of the tests which depend upon concentration of a dye or of urea or anything of that character. These tests are designed for estimating the function of a damaged kidney which is yet, anatomically, grossly normal, e.g., in chronic nephritis. In such a state the dye can be observed by the eye, almost *as it is secreted*, escaping from the ureter within a few seconds of the urine being concentrated in the tubules. If the dye has to make its way through a hydronephrotic kidney, or if it is diluted in residual urine in the bladder, the test becomes inapplicable and the findings meaningless. In such a case the only useful " dye " is iodine which can, *as it is secreted*, be visualised by X-ray.

2. Renal function may be found at the time of examination to be impaired by both (*a*) *ob*struction and (*b*) *de*struction of renal substance. *There is no renal function test available to draw a clear distinction between these two factors.* The severity of the renal damage, if any, must be judged on clinical grounds as well as on tests of renal function. Similarly, the capacity of the kidney for recovery must be judged on clinical grounds as well as laboratory findings.

The following are the standard useful tests in prostatic obstruction :

1. *Blood urea or its equivalent.* This is not a very sensitive test and a normal figure may be obtained in the presence of quite marked pathology. A raised blood urea therefore means that something is definitely wrong. The level of the blood urea does not indicate whether the trouble is purely obstructive and therefore wholly recoverable or whether it is due to a combination of obstruction and destruction. In general the following figures may be taken as reliable guides in prostatic obstruction :

Up to 40 mgm. %	Unlikely to be much renal damage and complete recovery probable.
40 to 60 mgm. %	Unlikely to be much renal damage and complete recovery probable—but less certain.

60 to 80 mgm. %	Hydronephrosis almost certain. Some degree of renal damage probable.
80 mgm. % and over	Some degree of renal damage highly probable.
150 to 250 mgm. %	Renal damage almost certain. Complete recovery highly improbable. Condition almost certainly neglected.
Over 250 mgm. %	Condition certainly neglected and of long standing. Acidosis, anaemia and oedema all highly probable. Complete recovery of renal function almost out of the question.

When deductions have to be drawn from a single sample of blood, the clinical history and clinical condition help in deciding whether, for example, there is likely to have been a sudden sharp rise in the urea content or a state of chronic renal damage. In recent acute obstruction, the figure mounts steadily from day to day but falls sharply from hour to hour when the obstruction is relieved. By contrast in chronic retention the relief of obstruction may be followed by a rise in the blood urea if adequate hydration and blood pressure are not maintained.

Serial readings are an essential guide to progress.

2. *Intravenous pyelography*. This investigation is probably quite safe whatever the blood urea but it is likely that no shadow will appear in patients with a blood urea of 100 or more. The test should be carried out whenever possible in prostatic obstruction and the following valuable scale of assessments may be made :

(*a*) Kidneys normal.

(*b*) Moderate degree of hydronephrosis.

(*c*) Gross hydronephrosis or no demonstrable function, also

(*d*) The density of the bladder shadow, making allowance for dilution with residual urine, gives an indication of the total renal function even when the kidneys cannot be well visualised.

(*e*) The size of the bladder shadow after micturition is a guide to the amount of residual urine.

(*f*) A filling defect in the base of the bladder may be seen if the prostate is very large, diverticula may be seen and, rarely, an unsuspected growth revealed.

(*g*) Progress can be observed after operation in the shrinkage of hydronephrosis and the disappearance of residual urine.

3. *The CO_2 combining power* should be done in all cases of severe chronic retention, because the retention of acid radicles can produce a severe degree of acidosis. Whilst this may, in itself, be a threat to life, it is also an indication of a serious degree of urinary retention or renal failure or both.

. A *blood count* is necessary in bad risk cases on specific as well as general grounds, because the chronic retention of waste products is frequently associated with an important degree of secondary anaemia.

5. *Water concentration and dilution* can be assayed over long periods in patients who are not urgently ill. The test is not ordinarily useful in prostatic subjects but may be so on occasion. A specific gravity constantly around 1,010 with a urinary urea constantly in the region of 0.8 to 1 gm.% indicates severe impairment of renal function but offers no evidence as to whether this is irreversible or simply due to obstruction and therefore capable of full recovery. Any gross departure in either direction from these levels proves that the kidneys retain their power of adaptation to different circumstances and that they are working under conditions which permit them to exercise that power.

DIAGNOSIS AND MANAGEMENT OF PROSTATIC OBSTRUCTION

Since benign senile enlargement is by far the commonest lesion, it is convenient to base the discussion on this condition.

BENIGN SENILE ENLARGEMENT

Clinical features

1. *Increased frequency* of micturition is the rule even when there is no gross residual urine. Sometimes this is the only complaint. Very occasionally there is no increase in frequency even in the presence of a large amount of residual urine.

2. *Dysuria* is almost invariable, the stream being slow to start and poor in strength. Urgency is common, sometimes with involuntary micturition, especially in sleep.

3. *Acute retention* is sudden, painful and greatly distressing. The bladder is palpable and tense. In all cases of retention, the prostate may be obscured on rectal examination.

Acute retention often occurs as a complication of some systemic illness such as pneumonia or cardiac failure.

4. *Chronic retention* is partial retention, its counterpart being residual urine. Some water is passed but a significant amount is retained. Chronic retention may be discovered for the first time in the course of some other systemic illness or on routine examination.

Chronic Retention presents in four ways :

(*a*) *Silent* retention with or without renal damage. The patient is unaware of the state of his bladder. Back pressure changes are usual, but from time to time patients are seen with grossly distended bladders, little in the way of symptoms and healthy kidneys.

(*b*) *Retention with overflow* incontinence, especially in sleep, when the sphincters relax. Renal damage is usually advanced by the time overflow incontinence occurs.

(*c*) *Partial retention* becoming *complete*. This very important problem is discussed in some detail presently.

(*d*) *Retention with uraemia*. This occurs as a later stage of one of the preceding states but is most particularly insidious in the case of silent retention, i.e., initially without symptoms but ultimately with severe renal damage. Patients in this state may present with symptoms suggesting carcinoma of the stomach, profound anaemia, intestinal obstruction, etc.

5. *Haematuria* is quite common and is characteristically terminal or initial. Very occasionally there is urethral bleeding apart from micturition.

Differential diagnosis

The competent surgeon should very seldom make a mistake in the clinical differential diagnosis of benign prostatic obstruction. Apart from senile enlargement, the likely sources of error, in order of frequency are :

1. *Carcinoma of the prostate*. The total history is one of months rather than years and the age of incidence is often below the " prostatic " age. On rectal examination the gland is irregularly hard and the median sulcus is often lost or replaced by a ridge of growth at the site of the posterior lobe, running into the membranous urethra.

2. *Marion's disease—Protatisme sans prostate*. The history is usually of decades, rather than years : micturition may have been noticeably slow since schooldays. Very gross changes in the upper tract may be demonstrable despite apparently excellent health. Diverticulum of the bladder is a common concomitant. The prostate is so small as to be impalpable (but even a big prostate may be difficult to palpate when the bladder is distended).

3. *Small fibrous prostate* is suspected on palpation in the " cold " case. In retention, whether acute or chronic, it may be difficult to distinguish from senile enlargement, and there is no reliable distinguishing characteristic in the history. The distinction between the two conditions is important only if the surgeon adopts a different method of treatment (e.g., resection instead of open operation) in such cases. The point is dealt with later under cystoscopy.

4. *Calculous disease* is revealed by X-ray.

5. *Urethral stricture* practically does not arise as a point in differential diagnosis because the patient who has a stricture of such antiquity as to simulate prostatitic enlargement knows all about it and is at pains to give his doctor the benefit of his knowledge. Moreover, senile enlargement of the prostate does not, for practical purposes, occur in patients who have had a urethral stricture under treatment. This is the only known prophylaxis against prostatic enlargement !

6. *Central nervous disease*, e.g., tabes dorsalis or disseminated sclerosis, is again a condition of which the patient is usually already aware. However,

a routine superficial examination of the C.N.S. is never to be omitted. It is to be remembered that prostatic enlargement may complicate these conditions.

7. *Carcinoma of the bladder*, stone, etc. These conditions seldom simulate prostatic enlargement but may complicate it. After consideration of every other approach, the need for cystoscopy arises and is discussed below.

INVESTIGATION OF THE "COLD" CASE

1. The *general examination* includes the C.N.S., C.V.S., etc., and especially a check on mental stability. The unstable patient may prove almost unmanageable after prostatectomy. Large parenteral doses of vitamin B complex may then be very helpful in such cases.

2. *Renal function* (*vide supra*).

3. *Mid-stream specimen of urine*. A catheter should *never* be passed simply for the collection of a specimen of urine and least of all in a patient with residual urine in whom contamination is certain to lead to infection which may prove disastrous. The specimen is cultured and sensitivity tests carried out. The urea content and specific gravity are estimated.

4. *Estimation of residual urine* may be made by bimanual examination and by I.V.P. The precise *measurement* of residuum by catheterisation after micturition is useless and dangerous: useless because it is the *effects* of retention that are significant, not the precise *amounts*: dangerous because of the peculiar risk of infection from contamination in such cases. This applies with especial force in Marion's disease in which the efficacy of operation is always in doubt and the advisability of interference a matter for careful debate. It may be too late to withhold surgery once infection has been introduced.

5. *Cystoscopy*, like catheterisation, may aggravate the prostatic condition by trauma and contamination. The importance of these two factors is least when the examination is carried out immediately before the definitive operation, at the same operative session under the same anaesthetic.

Diagnostic cystoscopy, at any other time, in prostatic subjects, should be strictly avoided.

INDICATIONS FOR OPERATION

There are three indications for surgery which should never be confused. They are:

(i) *The conservation of renal function*. In general, this applies in the patient with chronic retention and back pressure changes, and in particular to any patient with recognisable renal damage due to obstruction.

(ii) *The convenience and comfort of the patient*. This applies in the patient who has frequency or dysuria, or both, but a healthy upper urinary tract. Sometimes a patient in this group is influenced by the fear of passing into

the first group when he is older and less able to withstand the operation. Other patients pass from the second to the first or third group whilst under observation.

(iii) *The occurrence of complete retention.* This is very seldom an isolated incident and is usually an indication for prostatectomy. Only in exceptional circumstances (e.g., after operation for some other condition, in an acute illness of another character or after a severe and prolonged chill) should it be accepted as an incidental happening and relieved by catheterisation without having definitive operation in mind.

MANAGEMENT

The principles of treatment (as opposed to techniques) appropriate in different circumstances are tabulated below :

1. *In the average good risk case.* The definitive procedure favoured by the surgeon concerned should be carried out as soon as convenient, in one stage.

2. *In acute retention.* This is a condition urgently demanding relief and a practitioner in the country may have to pass a catheter despite the known risks. Assuming no instrument has been passed, the surgeon is faced with the choice of prostatectomy at once in a sterile field or of contaminating the field by preliminary drainage. Painful, acute retention is unlikely to be a sequel to chronic obstruction. If the patient has grave constitutional illness apart from the urinary obstruction, there is a good case for temporising. If he is otherwise fit the advantages are all on the side of immediate and clean radical surgery. Administrative difficulties may necessitate a single catheterisation which should not be repeated. Some prefer, if necessary, to empty the bladder once with a lumbar puncture needle suprapubically.

3. *In chronic* (incomplete) *retention.* There is no urgency and time can be spent in preparing the patient for operation. The blood urea may be brought down with free fluids, acidosis may be corrected by the elimination of sulphate and phosphate radicles and the administration of base, anaemia can be corrected and so forth. When the best preparations have been made, the surgeon faces the same choice as before : either a clean one-stage or a septic two-stage procedure. All the points in favour of clean radical surgery in acute retention are of greater, much greater, importance in chronic retention, where the damaged upper tract is open to the ascent of infection.

Whatever the procedure adopted, the needs of the patient in the post-operative period are paramount if lives are not to be lost. The post-operative management is all important.

If preliminary drainage is decided upon, either a Gibbon or a small Foley catheter should be used and ambulation maintained. *The post-drainage management is similar to and just as important as post-operative management* if the bad-risk case is to be brought to definitive surgery.

After preliminary drainage, nothing more than a Freyer's prostatectomy should ever be attempted, because the field is septic and sepsis must not be disseminated by prolonged retraction and manipulation or the opening up of tissue planes. Moreover, free drainage of the bladder through a suprapubic tube is obligatory in such an infected case. To ignore these facts is to run counter to basic general surgical principles.

4. The sick man in whom *incidental retention* develops is treated by catheter drainage as in (3) above.

5. *When complete retention supervenes on chronic partial retention.* This is the real dividing of the ways in the policy to be adopted. Since there is complete retention *something* must be done at once. There are only two possibilities :

(*a*) Immediate prostatectomy.

(*b*) Preliminary drainage—by whatever means.

In the choice between these procedures there is little to be added to what has already been said. *Preliminary drainage* has all the appearance of caution but introduces infection which may (i) cause early death, or (ii) *fail* to improve the azotaemic state and which in any case (iii) leaves an infected field for the definitive operation. Against these risks it is necessary to consider the possible advantages. In theory the patient can be " prepared " and " got fit " for operation. In fact and in practice there is very seldom anything to be done except wait between drainage and prostatectomy. If there is any demonstrable gross disease elsewhere that needs correction the whole picture is altered and in such a case preliminary drainage may be justified.

Immediate prostatectomy in this type of case has the merit of getting rid of the obstruction in a clean field at the beginning of the course of treatment. Thereafter, all is convalescence rather than preparation for an ordeal. But the details of after-treatment as described below are extremely important.

6. In *carcinoma with chronic retention*, oestrogen therapy is instituted. Catheterisation and cystoscopy should be assiduously avoided.

7. In *carcinoma with complete retention*, a Foley catheter is passed and oestrogen therapy instituted.

In most cases of carcinoma, 5mgm. of Stilboestrol t.i.d. gives relief. If necessary the dose is increased up to even 100 or 200 mgm. t.i.d. Honvan (phosphorilated oestrogen) may be given parenterally and later by mouth in resistant cases, of which it is said to benefit a percentage. More information is needed on this score. Orchidectomy or evisceration of the testicles is advisable in patients who either fail to respond to hormones (about 10 per cent.) or who tolerate them poorly. A patient who has failed to respond to hormone treatment is, however, unlikely to do well with orchidectomy. Adrenalectomy and hypophysectomy have proved disappointing and are not generally employed.

When the hormonal response is good, the severe pain of bony secondaries disappears very rapidly indeed and a raised serum acid phosphatase returns towards or to normal. The prostate softens and shrinks and the condition remains under control, on maintenance dosage, for months or years. The period of relief is unpredictable and may be many years.

DEFINITIVE PROCEDURES

1. *Transurethral resection* whether by cold punch or by diathermy loop is favoured by some surgeons for a wide range of cases. Most surgeons reserve the method for small adenomas, fibrous prostates, Marion's disease and carcinoma. The technique is not discussed further in this article.

2. *Retropubic prostatectomy* is not favoured by the present writer because it seems to invite certain untoward sequelae. The prostatic plexus of veins is disturbed, with the risk of spreading thrombosis in association with infection of the extensive retropubic connective tissue space of Retzius. Moreover, the capsular sutures carry infection into the urogenital diaphragm and thence to the periosteum with the production of osteitis pubis. For these reasons the operation should, in the writer's opinion, never be considered except as a strictly aseptic one-stage procedure and even then is liable to be followed by the complications described, as a result of contamination per urethram in convalescence, of the content of the space of Retzius, whether it be blood, urine, or just serum.

The chief advantage of the operation is the absence of risk of developing a suprapubic vesical fistula. The facts should not, however, be overlooked that the occurrence of such a fistula may lessen the danger of other complications arising, and that such a fistula is not, in itself, a threat to life.

The retropubic route is most valuable when the prostate is very large and the bladder very small.

3. A *modified Wilson Hey operation* is sound in theory and practice but calls for great patience and care in its execution. Its essential points are as follows :

(*a*) The towels are so arranged that the suprapubic region is laid bare, the penis lies in a separate layer of towelling and the forefinger of the left hand may have access to the rectum without soiling the field.

(*b*) The bladder is opened widely by a suprapubic approach.

(*c*) After inspection of the bladder the ureteric orifices are identified, a Tiemann's catheter passed retrograde down the urethra and the proposed line of enucleation of the " adenoma " demarcated with a diathermy cut.

(*d*) With the left forefinger in the rectum for support, the right forefinger enters the prostatic urethra. The anterior commissure is broken by forward pressure and then each lateral lobe is freed in front and laterally until its apex can be lifted into the bladder. The plane between " adenoma "

and normal gland tissue is followed with great care. The postero-lateral attachment of the lobes is left intact where the main vessels run.

(*e*) The retractors are re-inserted and the enucleation completed under vision, with deliberate division by diathermy of the floor of the urethra just proximal to the verumontanum.

(*f*) The internal sphincter is deeply divided at 3 and 9 o'clock (Fig. 1). and haemostasis secured at these points. Haemostasis is also secured postero-laterally and at all other bleeding points. This is not always easy and may take twenty minutes or more.

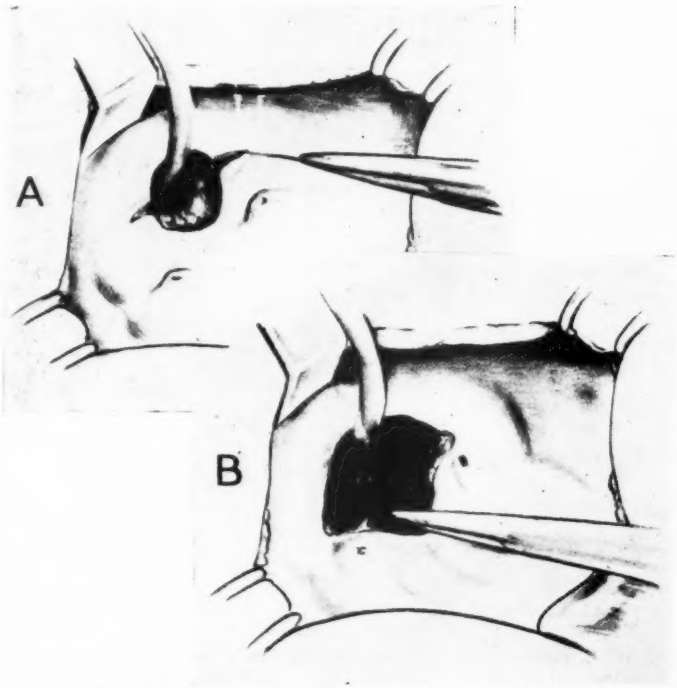


Fig. 1. (*a*) Bilateral internal sphincterotomy with diathermy. (*b*) Cavity opened out, haemostasis being completed.

(*g*) A two-way Portex tube is railroaded down the urethra and fixed with a Harris stitch and the bladder closed (Fig. 2).

If haemostasis is unsatisfactory, a suprapubic tube drain is used for twenty-four hours. This is best brought out through a blunt stab in the wall of the bladder, made with a haemostat to one side of or above the main incision. The resulting separation of the decussating fibres

closes very rapidly when the tube is removed and the suture closing the bladder is not interrupted. The space between the bladder and the abdominal wall is drained for twenty-four hours in all cases.

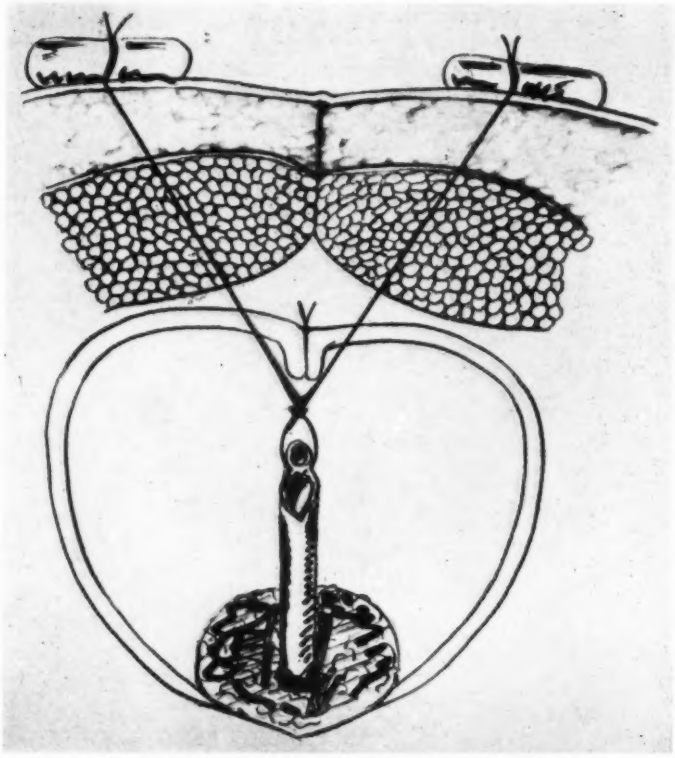


Fig. 2. Fixation by Harris stitch of Portex tubing with double lumen.

(*h*) The vasa are divided at the neck of the scrotum, the vesicular end of each being brought out as a vasostomy, to exclude the risk of epididymitis (Fig. 3).

4. *Freyer's operation* is possibly still the method used by the greatest number of operators. The steps of the operation are as follows :

(*a*) A limited suprapubic incision is made into the bladder which is held by sutures so that it does not fall away from the abdominal wall.

(*b*) The left forefinger is placed in the rectum to support the gland which is enucleated by the right forefinger, beginning in the way described in the last section. When the lateral lobes are freed, the urethra is deliberately

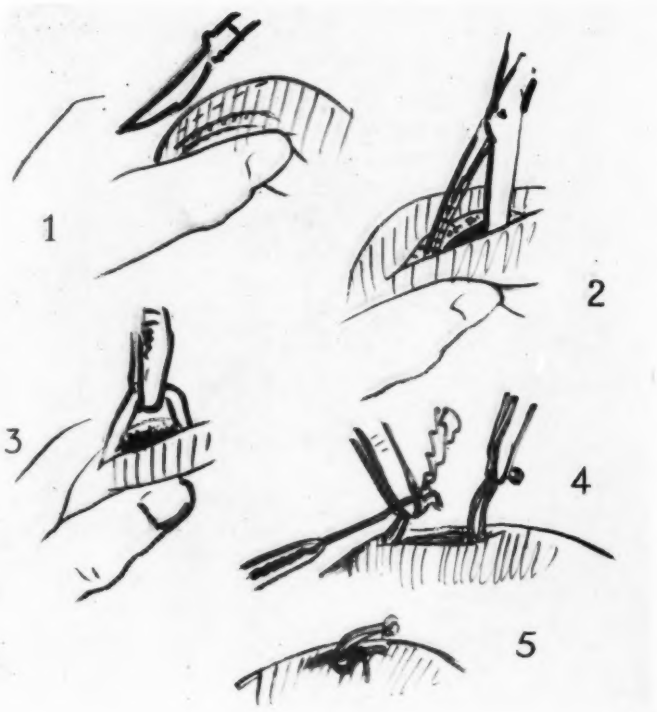


Fig. 3. Vasostomy.
(1) Vas supported by finger and thumb and cut down upon. (2) Space opened with haemostat. (3) Vas picked up with toothed forceps. (4) Distal end cauterised. (5) Proximal end exteriorised and sutured in position.

torn across as far proximally as possible, so as to avoid avulsion of its membranous portion. The circuit of the gland is then completed posteriorly so that the whole of the adenomatous portion is free and can be removed from the bladder.

(*c*) Hot saline irrigation of the prostatic cavity is carried out. If bleeding is not reasonably well controlled, the prostatic bed should be massaged p.r. to encourage its walls to contract down. *The neck of the bladder should in no circumstances be divided* as this upsets the normal haemostatic effect of its contraction. If a diaphragm develops after the operation, as it may in about 10 per cent. of cases, this should be dealt with as a separate problem.

(*d*) A generous tube is drawn through a blunt stab above the main

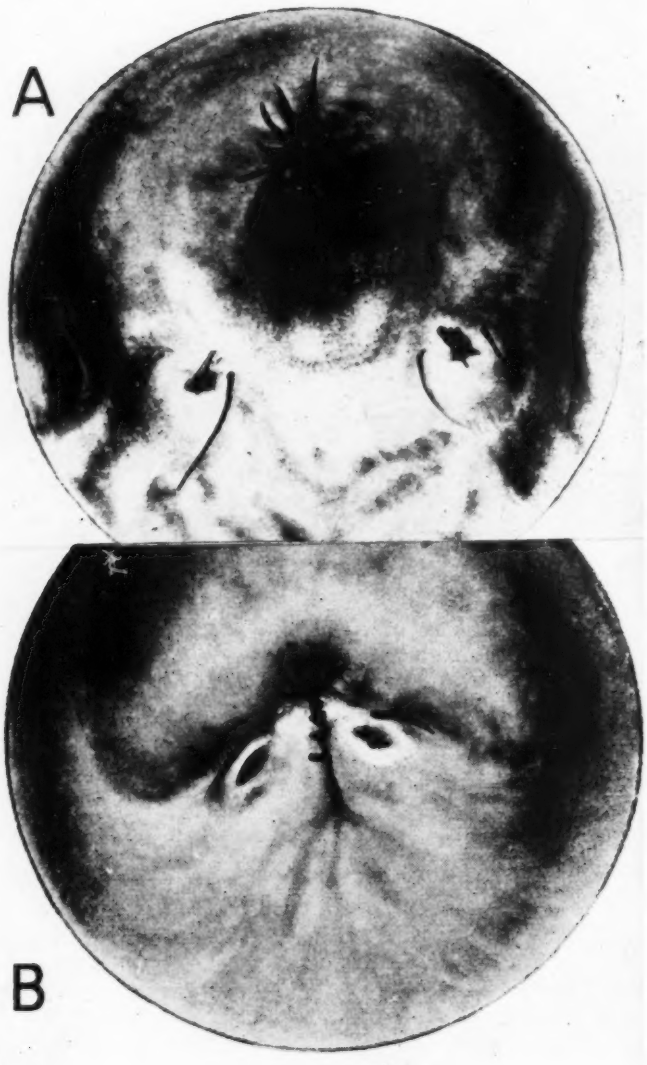


Fig. 4. Marion's disease.
(*a*) Characteristic appearance, the urethral orifice far forward from ureteric orifice.
(*b*) Recurrence of bladder neck obstruction after trigonectomy.

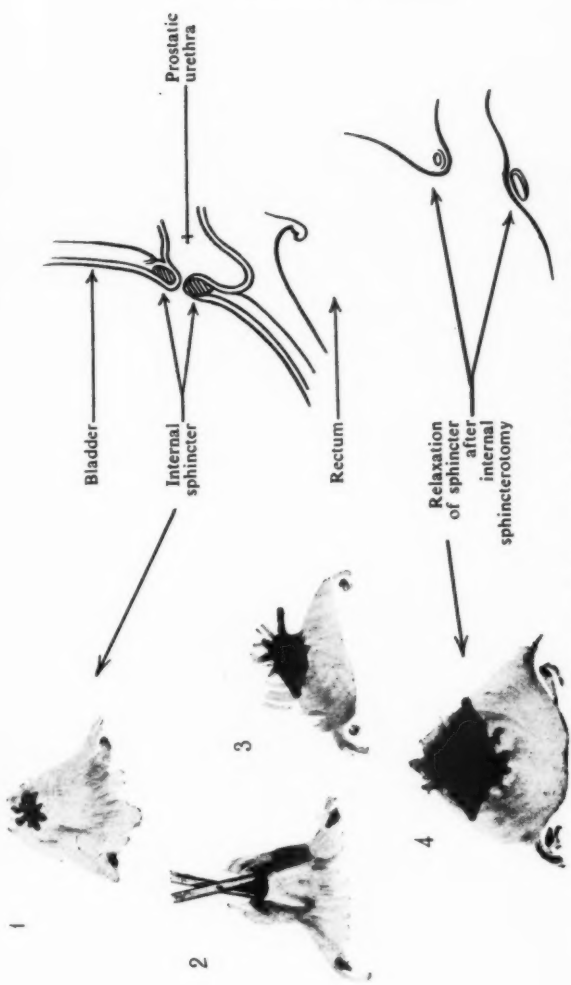


Fig. 5. Marion's disease and its relief by bilateral internal sphincterotomy.

1. The internal meatus.
2. Demonstration with haemostat of obstructing shelf.
3. Internal sphincterotomy completed on left and begun on right.
4. The resultant opening up of the internal meatus.

Scheme of profile view of Marion's disease. Note shelf formed by sphincter between prostatic urethra and trigone. This disappears after internal sphincterotomy.

incision in the bladder, well away from the symphysis, and the main incision is closed. The pre-vesical space is drained for twenty-four hours.

(*e*) The suprapubic tube is given sump-suction drainage for about forty-eight hours and then changed for a smaller one.

5. *Sphincterotomy* is extensively practised for the relief of Marion's disease. Transurethral resection is often effective but must be performed

with caution because the neck of the bladder may easily be transgressed, there being no prostatic bulk and no visible change from " adenoma " to capsule. Marion himself described trigonectomy with the diathermy knife as employed by Wilson Hey in his original method of prostatectomy. In the writer's experience this procedure is too often followed by the sides of the wedge-shaped incisions falling together and scarring of the trigone with an end result worse than that for the relief of which the procedure is undertaken (Fig. 4).

If internal sphincterotomy is to be employed at all, it is probably best to employ the writer's method. In this the muscle of the bladder neck is incised deeply at 3 o'clock and 9 o'clock and haemostasis secured with

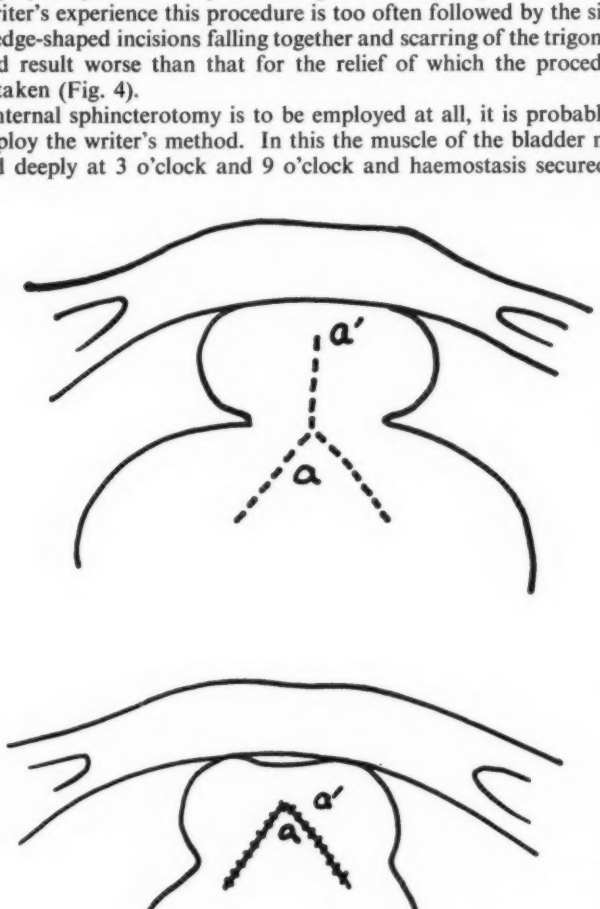


Fig. 6. V-Y advancement of a bladder neck by the retropubic approach for the relief of Marion's disease. The bladder neck and the whole prostatic urethra is enlarged.

(Based on a personal communication from Mr. Innes Williams.)

diathermy. The backward pull of the trigone opens the bladder neck and sides of the cuts do not tend to fall together as they do in trigonectomy (Fig. 5).

6. *Bladder neck advancement* by V-Y, via the retropubic route is probably the best operation for Marion's disease.* The internal sphincter is divided in the midline anteriorly and a tongue of bladder wall carried down into the anterior capsule of the prostate to increase the circumference of the neck of the bladder and the prostatic urethra permanently (Fig. 6).

7. *Diverticulectomy* should, when necessary, be carried out at the time of the definitive operation, immediately before the prostatectomy. The wide opening of tissue spaces calls for ample drainage. Preliminary drainage, always to be deplored, must be assiduously avoided in the presence of a diverticulum.

Post-operative care

Although different cases call for different handling, a number of points in treatment can be emphasised with advantage.

(*a*) Closed bladder drainage should be kept as clean as possible by the use of a Lane's bottle or some similar device.

(*b*) Continuous irrigation with 5 per cent. sodium citrate for twenty-four to forty-eight hours through the second channel of the Portex tube usually avoids clot retention and the need for intermittent emergency irrigation of the main channel, with its inevitable risk of contamination as a result of taking-down, syringing and reassembling.

(*c*) Some chemotherapeutic and antibiotic cover is advisable for about five days because of the high risk of contamination during this period. Penicillin and a sulpha drug are advised.

(*d*) About five days after operation, acid sodium phosphate is given, sufficient to produce and maintain an acid reaction, which discourages encrustation of the prostatic cavity and so reduces the incidence of secondary haemorrhage.

(*e*) Fluids, glucose and electrolytes are given intravenously for a few days in all but the simplest cases, because renal function must be briskly maintained and forcing fluids by mouth in old people leads to abdominal distension and vomiting.

(*f*) In poor risk cases, all the fluid from the bladder, plus any vomit or other discharge, is collected for each twenty-four-hour period, a sample taken and the total amounts of sodium and especially potassium are estimated. Corresponding amounts are returned to the body in the day's drip until such time as normal feeding can be begun. There is no other method of gauging the potassium requirements, which may be considerable, when diuresis is forced to eight or ten pints daily. It cannot be too strongly emphasised that diuresis of this order must be ensured by the

* The Author is indebted to Mr. Innes Williams for this description.

intravenous administration of corresponding amounts of appropriate fluid in patients with gross hydronephrosis and high blood urea (e.g., 150-300 mgm.%). If acidosis is corrected, electrolytes replaced and blood pressure maintained, diuresis occurs in response and in proportion to the fluid exhibited. Overloading with sodium causes dangerous degrees of water-retention ; potassium shortage causes muscular weakness, mental confusion and can be detected in the electrocardiogram. Oliguria and anuria result from hypotension and dehydration. If neither of these factors is the fault, and especially if there is sudden sharp fever, pyelonephritis is a likely cause of anuria and a broad spectrum antibiotic given intravenously will often produce an immediate diuresis. Failing such diuresis, the intravenous fluid intake is, of course, restricted at once to the daily need.

(*g*) Massage and movements, both passive and active, of the legs, breathing exercises and regular turning are begun on the day of operation and ambulation is encouraged as soon as the apparatus permits, preferably on the first post-operative day.

(*h*) The catheter is not removed from the closed bladder until it appears that the patient can safely and effectively empty his own bladder by the act of micturition. This may be anywhere from five days in the average case to five weeks in bad risk cases with gross hydroureters and hydronephrosis. Premature removal of the catheter in such a bad case is followed by the ureteric reflux of infected residual urine with consequent pyelonephritis which may easily prove fatal. The patient should be completely ambulant and able and willing to try to empty his bladder before the catheter is taken away. If, after removing the catheter, residual urine is suspected, this should be withdrawn each evening and, if necessary, the catheter replaced for a further period of continuous drainage.

(*j*) Suprapubic drains are removed or reduced in size as quickly as possible. The principle of sump-suction is employed so long as such drains are in position.

POST-OPERATIVE COMPLICATIONS

1. *Shock*. Arterial hypotension after prostatectomy is dangerous for two main reasons : it may lead to cerebral thrombosis or to supression of urine. On these accounts, spinal analgesia, in spite of its advantages in the technique of the operation, is probably better avoided. Blood loss should be made good and the circulating volume maintained.

2. *Primary and reactionary haemorrhage and clot retention*. Bleeding can be troublesome because of the blood loss involved—which is made good—and on account of the risk of clot retention. Continuous citrate irrigation, as described, may obviate the latter risk. If obstruction due to clots is suspected, the drainage tube should be " milked " or syringed in such a way as to demonstrate the presence or absence of a to-and-fro movement of the fluid content. Clots should then be cleared with a good suction syringe. Unfortunately, however, the extent of clotting can only be guessed. If the

trouble recurs, the two-way catheter may have to be changed. If there is still trouble, it is probably safest to take the patient back to the theatre with the least delay, re-open the bladder, clear out the clots and either re-suture or put in a suprapubic tube for twenty-four hours. Clearance with a Bigelow evacuator may be successful but is neither so sure nor so safe. Temporising measures with Foley catheters producing pressure in the prostatic bed are also too often unsatisfactory and dangerous.

With care at the time of operation, these accidents should occur but rarely. In the writer's unit where the modified Wilson Hey operation is routinely used, no patient has needed more than a change of catheter on this account for several years.

3. *Secondary haemorrhage.* This is caused by sepsis and is nearly always associated with an alkaline urine. Care to keep the urine acid is a sound prophylactic. If secondary bleeding persists, irrigations, and possibly suprapubic cystotomy may be indicated. Some workers carry out transurethral diathermy and find that the bleeding usually comes from one vessel only.

4. *Alkaline encrustation* is a concomitant of secondary haemorrhage. It is best treated by acid irrigation with Duke's apparatus or tidal drainage. Acid acetic B.P. 0.25 per cent. solution is appropriate.

5. *Urethral stricture* is liable to occur at the external meatus or the penoscrotal junction from the pressure of a too large catheter. In the latter situation a fistula may follow. Vulcanised red-rubber is more irritant to the urethra than latex rubber or plastic catheters.

6. *Bladder neck obstruction* does not follow the Wilson Hey procedure but is seen in some 10 per cent. of Freyer prostatectomies. It causes partial or complete urinary obstruction, with obstinate infection. If the bladder neck is passable, a transurethral resection is done. Otherwise open operation is called for. It is wise, therefore, to bear this condition in mind in patients who are not doing well. A massive block of scar tissue forms occasionally in cases in which a retropubic operation has fared poorly.

7. *Chronic pyuria* is attributable to encrusted cystitis, residual due to urethral stricture or obstruction at the bladder neck, diverticulum or retained foreign body or stone. Without one or other of these the infection should respond to appropriate treatment. It is important that there should be no residual infection at the end of the period of treatment and review —say three to six months. In most cases, infection will clear spontaneously within two to three months, if the conditions described are right. It is best to avoid, for some weeks therefore, antibiotics and drugs, other than those needed for acidification.

FOLLOW-UP

The patient is kept under observation and treatment until the urine is clear and sterile and the bladder emptying completely. Failure to

achieve these aims calls for inspection of the urethra for stricture, of the bladder neck for diaphragm formation or of the cavity of the bladder for an unsuspected diverticulum, a retained foreign body or for stone formation.

PROGNOSIS

Average to bad case—not greater than 2 per cent. mortality. Long term very good.

Very bad risk cases—mortality say 10 per cent. Long term very good, but blood urea may stabilize at 80 mgm. per cent. or higher and large fluid turnover may be needed to maintain good health.

Carcinoma—75 per cent. respond well and last for several years. Relapses late.

Marion's disease—relief from operation by no means certain. Carry on surprisingly well without operation if not infected in course of meddlesome " investigations."

Freyer's prostatectomy—approximately 10 per cent. bladder neck diaphragms need secondary resection.

All cases—occasional incontinence of unknown origin. Occasional failure to empty bladder in spite of apparently perfect result.

SUMMARY

The greatest emphasis in this lecture has been laid upon the following points :

1. The importance of asepsis and the manner in which preliminary catheterisation, cystoscopy and drainage deprive the patient of this advantage.
2. The unimportance of residual urine as such.
3. The value of the I.V.P. at all stages.
4. The fallacy in prostatic subjects of so many of the tests of renal function.
5. The need for simplicity of surgery in infected cases.
6. The retention of the catheter after operation until the patient is able to take over responsibility for the act of micturition.
7. The supreme importance of post-operative care in all its details.
8. The importance of the follow-up period.

RECENT OVERSEAS VISITORS TO THE COLLEGE

RECENT OVERSEAS VISITORS to the College have included Dr. Erik Thoresen from Trondheim, Norway, and Mr. and Mrs. Powell from New Zealand.

HYPOTHERMIA AS AN AID TO SURGERY

Lecture delivered at the Royal College of Surgeons of England
on
10th April 1958
by

D. N. Ross, F.R.C.S.
Assistant Thoracic Surgeon, Guy's Hospital

THE USE OF hypothermia in surgery is based on the observation that a reduction in temperature lowers the rate of metabolism and hence the oxygen consumption of the tissue cells. Since oxygen is transported to these cells in the blood stream, it follows that the blood supply to the cooled tissues can be reduced or cut off for limited periods without these cells suffering anoxic damage. The permissible time of circulatory arrest will depend on the susceptibility of the organs supplied to anoxia.

However, the first clinical application of hypothermia was based on quite a different line of reasoning. As far back as 1940 Temple Fay in the United States made the observation that secondary deposits from metastasising tumours were rare in the peripheral aspects of the limbs while being fairly common for instance in the shoulder girdle, pelvis and hips. He correlated this observation with the fact that the temperature of the limbs peripherally was perceptibly lower than proximally, and came to the conclusion that cold had an inhibiting influence on the malignant cell. On this basis he submitted a number of patients with widespread metastatic growths to prolonged but minimal degrees of reduced body temperature. The results were not encouraging, although a reduction in pain from bone secondaries was reported.

Sporadic attempts were subsequently made to use hypothermia as a form of therapy in schizophrenics, but it was not until Bigelow *et al.* of Toronto (1950) reported its use in dogs with arrested circulation and its possible application to cardiac surgery that it was thought of as a surgical tool. His writings were followed by a period of unfettered enthusiasm for "cold narcosis." The introduction of chlorpromazine and related drugs at this time resulted in anaesthetists throughout this country and the Continent using mild to moderate hypothermia in all manner of routine general surgical operations like gastrectomy, on the assumption that it conferred some ill-defined benefit or made poor-risk patients somehow safer for surgery. The increased clotting time of the cold blood and the tendency of the cold ventricles to fibrillate soon tempered this wave of enthusiasm and the indications and applications of the method are now reasonably well sorted out.

Nowadays for practical purposes we recognize three degrees of reduction of body temperature :

(a) *Mild* hypothermia—generally prolonged and with a reduction of temperature by 2 to 3 deg. down to say 33 to 34 deg. C.

(b) *Moderate* hypothermia which is the degree of cooling more generally used, and particularly in cardiac surgery. Here the reduction in temperature is by 6 to 7 deg. down to 30 deg.C.

(c) *Deep* hypothermia, generally below 25 deg.C. The use of temperatures in this range is largely experimental, with a view to total arrest of body or organ metabolism. Under this heading one may include the deep-freeze storage techniques for organs, blood vessel and corneal grafts, blood and sperms.

Hypothermic techniques

The method of inducing hypothermia will depend on the surgical application envisaged. Thus for prolonged mild hypothermia for say the hyperpyrexia associated with some head injuries we can induce moderate surface cooling with wet sheets and electric fans to aid evaporation. We must, in addition, take measures to knock out the body's reflex heat-conserving mechanisms of vasoconstriction and shivering (Fig. 1.). This is fundamental in achieving any degree of useful hypothermia and it can

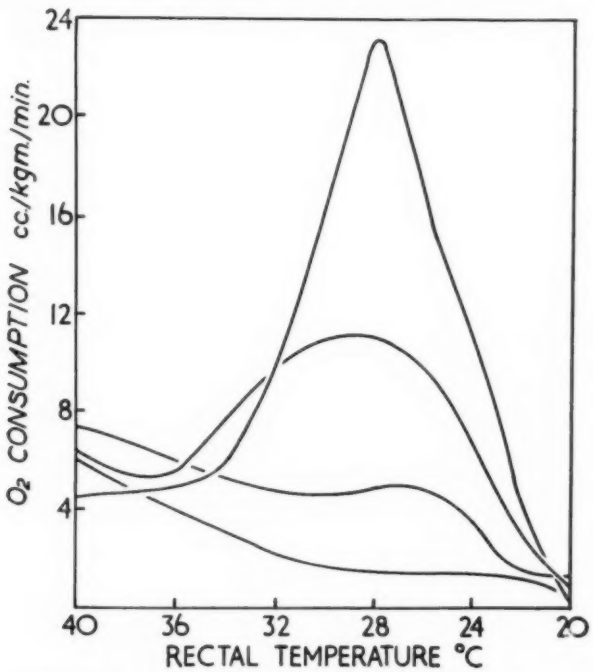


Fig. 1. Showing the effect of mild, moderate and gross shivering on oxygen consumption. Bottom curve—no shivering.

be brought about by means of very deep anaesthesia or light anaesthesia plus a muscle relaxant. But where prolonged hypothermia is planned the use of chlorpromazine combines the effects of a mild narcosis with peripheral vasodilatation, so that heat loss is facilitated.

For hypothermia down to 30 deg.C., either surface or blood stream cooling is used. The former is usually induced by supporting the anaesthetised patient on a canvas sling suspended within an ordinary bath. Water is added at room temperature to cover the trunk, after which ice is added

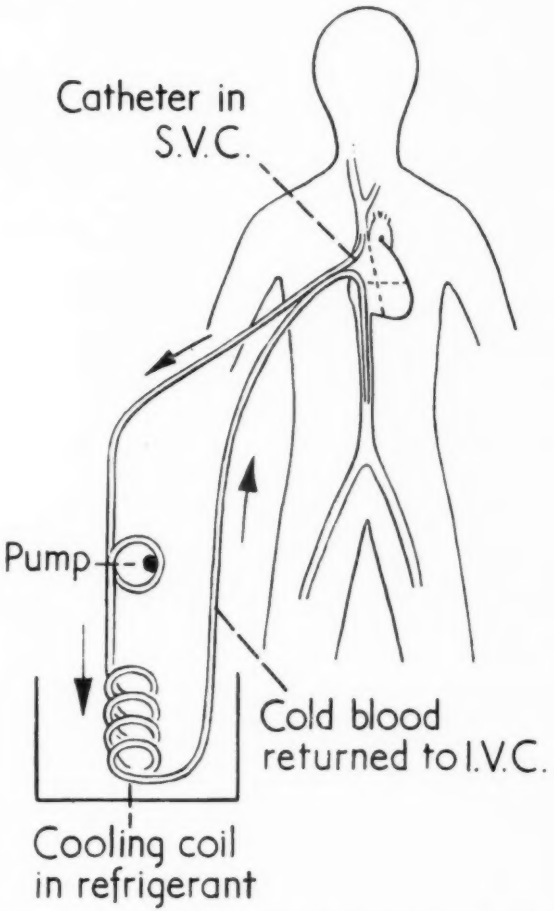


Fig. 2. Diagrammatic circuit of the course of the blood in blood-stream cooling.

to bring the temperature of the water down to about 9 deg.C. The hands and feet are left out of the water and measures are taken to prevent shivering with relaxants and chlorpromazine. At a body temperature of about 33 deg.C. the patient is removed from the bath and dried. The peripheral skin vessels then dilate and perfuse the surface skin and

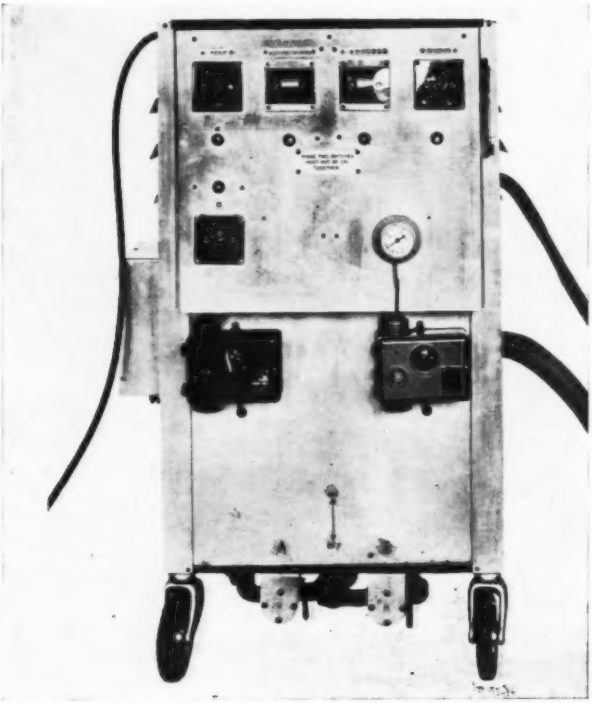


Fig. 3. Refrigerator unit for supplying source of refrigerant at −4 deg.C.

subcutaneous tissues bringing about a further fall of temperature known as the " after-drop," and by judging this skilfully the anaesthetists plan to have the patient's temperature at about 30 deg. C. when the surgeon is ready to arrest the circulation.

In cardiac surgery we feel there are advantages in opening the chest and exposing the heart before inducing hypothermia. We are then in a position to check the diagnosis and confirm the need for hypothermia or a heart-lung machine before proceeding further.

Cooling is then induced if required by cooling a proportion of the patient's blood in an external circuit and allowing the returning blood to

bring about the fall in body temperature (Ross, 1954) (Figs. 2, 3, 4). Hypothermia induced in this way is not subject to a further after-drop of temperature when cooling is stopped (Fig. 5), and the heart is under direct vision throughout so that arrhythmia can be immediately detected. Also rewarming can be brought about quickly at the end of the period of circulatory arrest by warming the blood in the extracorporeal circuit (Fig. 6).

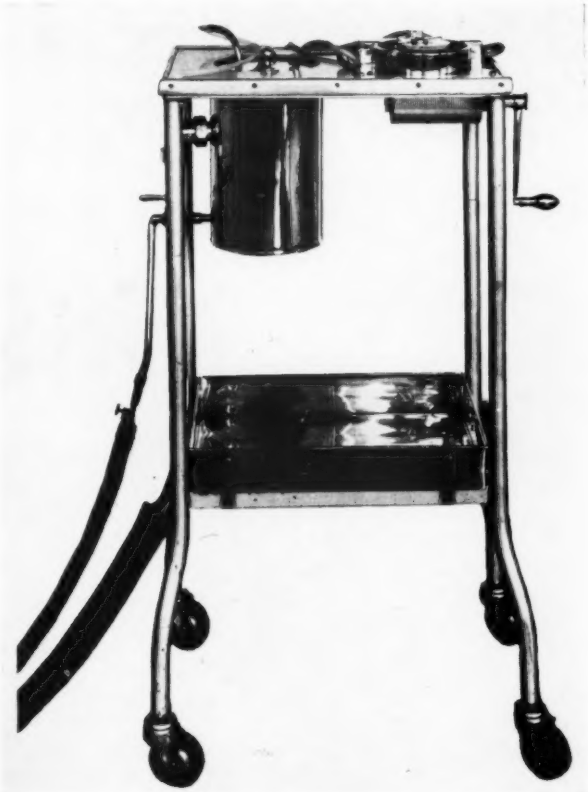


Fig. 4. Heat exchanger unit through which patient's blood is hand pumped.

Deep hypothermia with temperatures below 25 deg.C. can only be achieved with the aid of a heart-lung circuit, since the heart will go into spontaneous ventricular fibrillation or arrest within this temperature range.

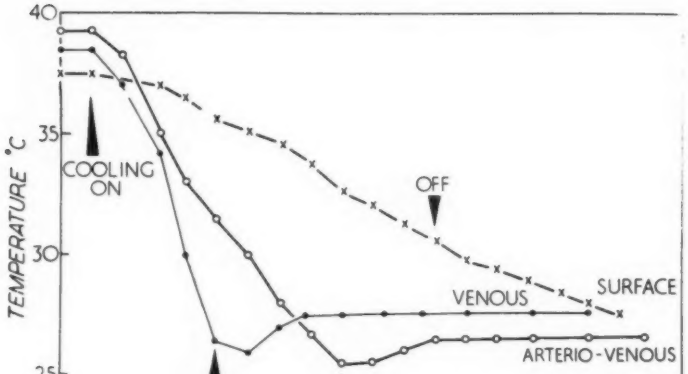


Fig. 5. Note continued fall of temperature (after drop) in surface cooling.

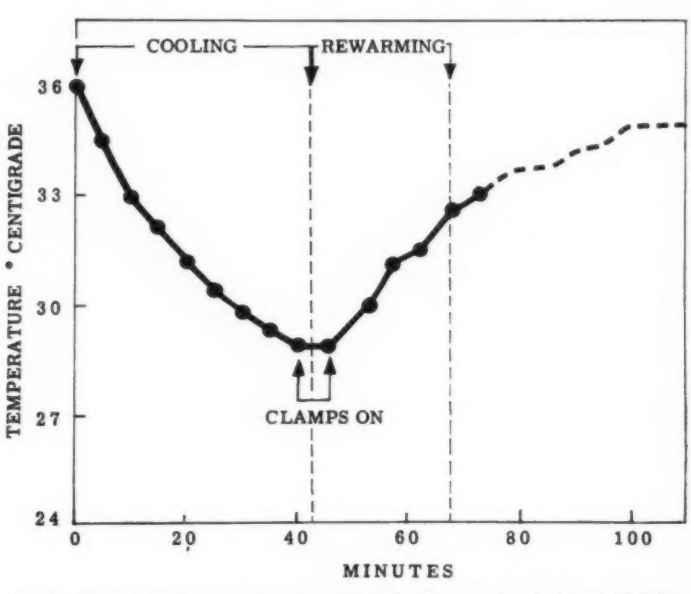


Fig. 6. Typical cooling and rewarming chart in closure of an atrial septal defect.

Very low temperatures for the storage of organs and blood vessels or blood require the use of freezing mixtures of CO_2 and alcohol with a temperature of about -80 deg.C., and glycerol is sometimes used ast he suspending medium to prevent the formation of ice crystals which would destroy the cells.

Practical applications

With regard to the practical surgical applications of hypothermia, the two main fields in which it is of use are cardiovascular and neurosurgery. The former includes the surgery of the heart and great vessels. With regard to the heart it is generally conceded that the total body circulation can be occluded for up to ten minutes at 30 deg.C. This limits the clinical applications to a fairly well-defined group of conditions. Uncomplicated atrial septal defects can certainly be closed within this time limit and this represents the commonest application of hypothermia in present-day surgery (Fig. 7). The average period of circulatory arrest for closure of an A.S.D. is five to seven minutes. Pulmonary and aortic valve stenosis can also be relieved under direct vision during hypothermic arrest of the circulation, but ventricular septal defects, whether occurring alone or in association with Fallot's tetralogy, require about twenty minutes of intracardiac surgery so that some form of heart lung circuit is used in these cases.

As far as the surgery of the great vessels is concerned—notably aneurysm of the aorta—it is normally safe to clamp the abdominal aorta below the renal arteries for at least two hours at usual temperatures but when resection above the renals is involved hypothermia is necessary to give protection to the kidneys, which would probably suffer damage after about thirty minutes.

For the resection of aneurysms of the thoracic aorta one has to remember the vulnerability of the spinal cord in clamping above say D 7 to 10 at normal temperatures and hypothermia is required under these conditions to avoid paraplegia. On the other hand a bypass shunt can be used to carry this blood during resection of the thoracic aorta at normal temperatures.

The second field in which hypothermia has a fairly wide application is neurosurgery and here it is theoretically possible to arrest the circulation temporarily to one or both cerebral hemispheres, in order to gain control of haemorrhage in resecting difficult vascular tumours or in the surgery of subarachnoid haemorrhage. In addition there have recently been favourable reports of the value of a reduced body temperature in preventing or minimising the post-operative pyrexia, coma and high mortality associated with neurosurgical intervention in the region of the hypothalamus and mid brain (for example in the removal of large craniopharyngiomas) (Inglis and Turner, 1957).

Mild hypothermia has a more widespread application in severe head injuries where there is frequently prolonged coma and high temperatures.

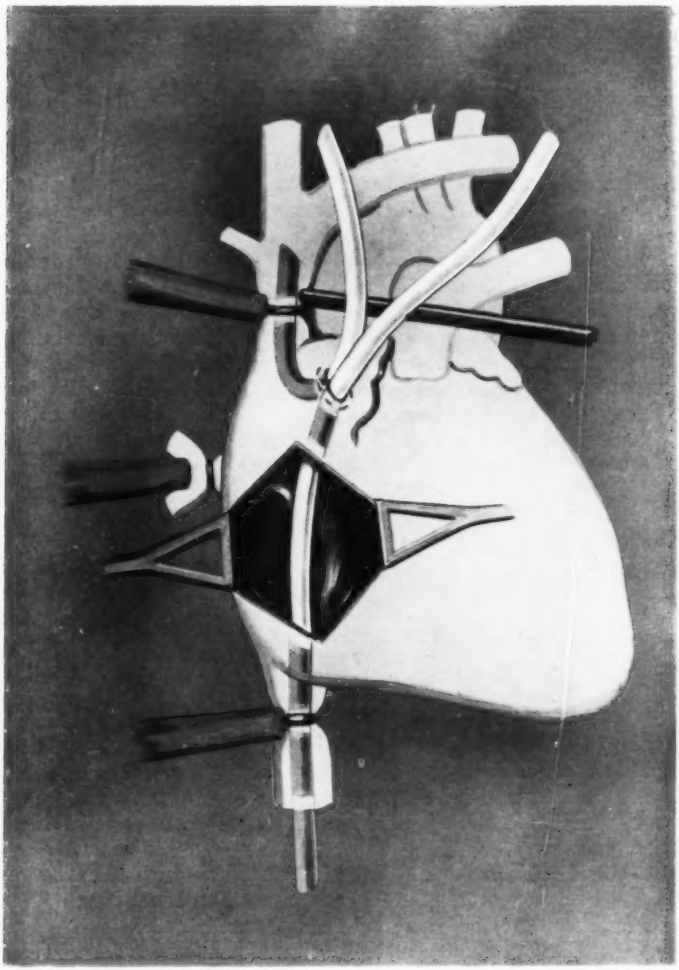


Fig. 7. Diagram showing snares and clamp on great vessels in closure of A.S.D.

Hypothermia is known to reduce the brain volume (Rosamoff, 1956) and it may exert its beneficial effects under these circumstances by limiting the development of damaging cerebral oedema. It is sometimes necessary to maintain a reduction of one to two degrees centigrade for days.

A more recent application of hypothermia which is partly neurosurgical and partly vascular is in the removal of atheromatous plaques and

thrombi from the origin of the internal carotid artery. A plaque of atheroma in this site gives rise to a characteristic syndrome of recurrent strokes of hemiplegia with associated blindness on the opposite side. The blindness is of course due to the interruption of the blood flow in the ophthalmic branch of the internal carotid, while the ischaemia of the anterior and middle distribution produces the contralateral hemiplegia. These plaques can be removed by endarterectomy of the carotid bifurcation. Since the opposite carotid is likely to be involved it is safer to occlude the affected common carotid under hypothermia rather than to rely on a cross-circulation from a diseased vascular tree.

Other applications of hypothermia are of a minor nature and often

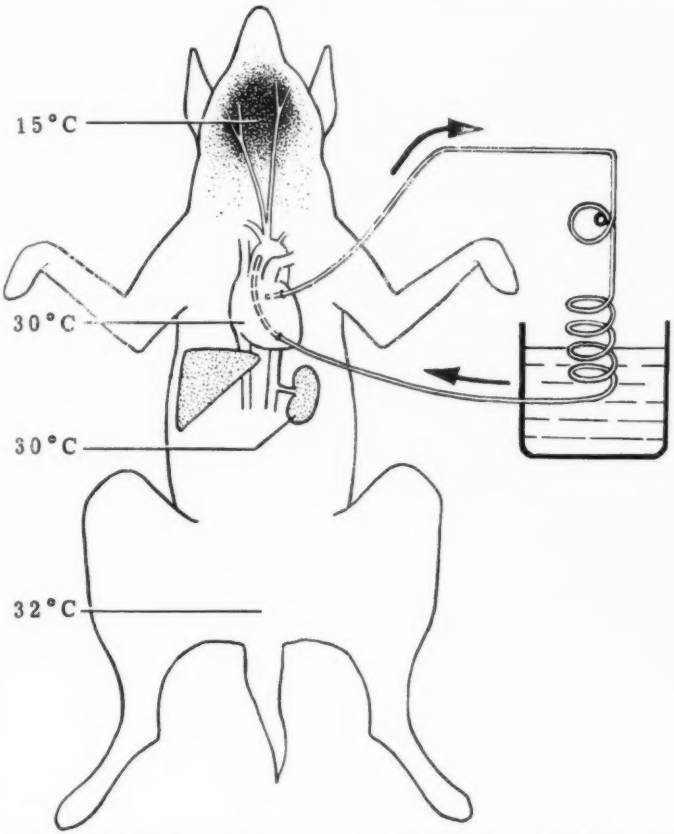


Fig. 8. Experimental method of producing selective cooling of brain with catheters in left atrium and aortic arch.

have more theoretical than practical advantages to offer. For example it has been said to be of value in severely cyanotic cases in reducing their oxygen requirements. However, apart from increasing the danger of ventricular fibrillation it increases the bleeding tendency which in these polycythaemic children is already considerable. Again it has been suggested as a form of therapy in severe shock and as a preliminary to surgery in severe thyrotoxicosis. Few people would be prepared to deliberately cool a shocked patient and there are easier methods of reducing thyrotoxicosis pre-operatively. The technique has a definite but limited application in infections in young children which are likely to be associated with a damaging and uncontrolled hyperpyrexia sometimes 105 to 106 deg. F. and perhaps associated with convulsions. An ingenious form of gastric cooling has been introduced for these cases in which the central body temperature is reduced by means of a thin rubber balloon in the stomach. Perfusion of the balloon with cold water maintains the child's temperature within normal limits (Khalil and MacKeith, 1954).

With regard to the future of hypothermia in surgery, the vulnerability of the myocardium at temperatures below 28 deg.C. effectively limits the application of lower temperatures which would permit longer periods of circulatory arrest. If a chemical means of arresting or depressing cerebral metabolism can be developed (as potassium reversely affects the heart's

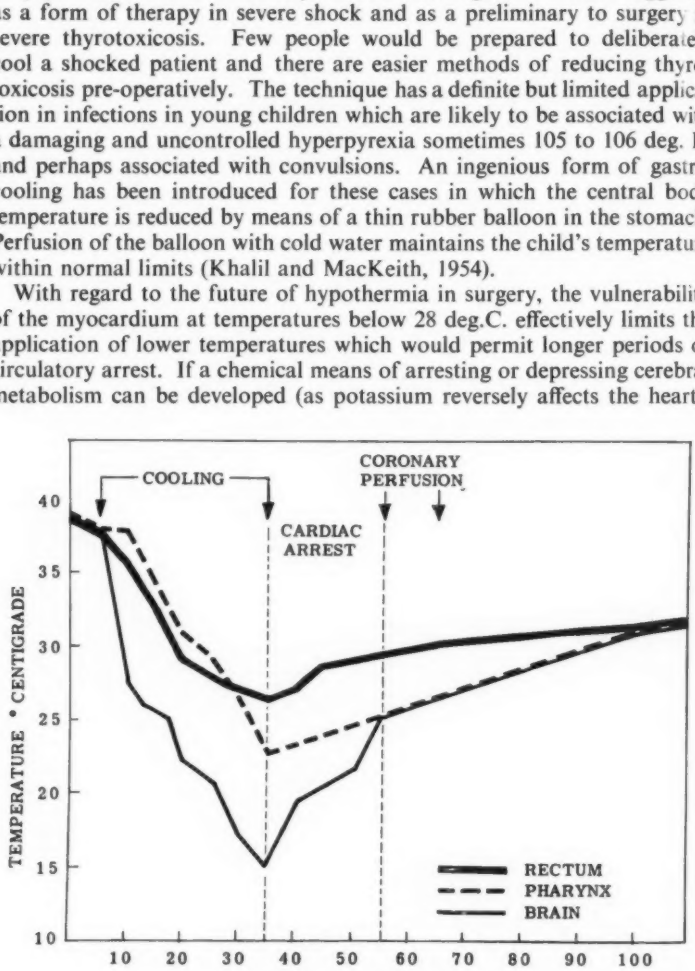


Fig. 9. Chart showing fall of brain temperature to 15 deg.C. while rest of body is at a temperature of 28 to 30 deg. C.

action), then it should be possible to dispense altogether with the tedious ritual involved in inducing clinical hypothermia.

Attempts have been made to extend the range of hypothermia by combining it with a low-flow heart-lung machine in the hope that a smaller simpler machine will maintain the circulation under conditions of cooling.

Also experiments have been carried out on selective brain cooling in order to achieve prolonged hypothermic protection of the brain without arresting the heart or precipitating ventricular fibrillation. These experiments are continuing (Figs. 8 and 9).

With regard to very low temperatures below zero centigrade such as those that have been used for the storage of blood cells and whole organs in a viable condition, we are here just on the threshold of an era of organ replacement in surgery. A stored lung, lobe, kidney or even heart, will then be available for replacement of the diseased organ. As a technical exercise these organ replacements have been performed on innumerable occasions but their permanent acceptance by the host depends on solving the complex problems of tissue compatibility and antibody reactions.

REFERENCES

BIGELOW, W. G., CALLAGHAN, J. C. and HOPPS, J. A. (1950) *Ann. Surg.* **132,** 531.
FAY, T. (1940) *N. Y. S. J. Med.* **40,** 1351.
INGLIS, J. M., and TURNER, E. (1957) *Brit. Med. J.* **1,** 1335.
KHALIL, H. H., and MACKEITH, R. C. (1954) *Brit. Med. J.* **2,** 734.
ROSAMOFF, H. L. (1956) *Proc. Roy. Soc. Med.* **49,** 358.
ROSS, D. N. (1954) *Lancet* **1,** 1108.

DONATIONS

DURING THE PAST month the following generous donations have been received :

Restoration and Development Fund:

£5,000	The Miriam Sacher Charitable Trust (further donation).
£100 p.a. for 7 years	Sir Henry Souttar (under covenant).
£15 p.a. for 7 years	A. D. Harper (under covenant).
£7 10s. p.a. for 7 years	W. G. Gill (under covenant).

Down House:

£375	The Carnegie U.K. Trust (further donation).

Appeal Fund:

The following Fellows have generously undertaken to make voluntary annual donations to the College for seven years under covenant :

H. I. Deitch, C. V. Patrick, R. G. Pulvertaft, J. C. Ross, J. K. Ross, Sir James Paterson Ross, M. J. Smyth.

VARIATION AND SELECTION WITHIN TUMOUR CELL POPULATIONS

Imperial Cancer Research Fund Lecture delivered at the Royal College of Surgeons of England

on

13th May 1958

by

D. C. Roberts

Research Histopathologist, Imperial Cancer Research Fund

DESPITE ADVANCES IN the art and science of surgery through the years, the results of treatment of neoplastic disease still leave much to be desired. In an effort to provide alternative and supplementary methods of treatment, much effort has been applied to the finding of chemotherapeutic agents against cancer.

The chemical control of cancer has not yet been achieved, but progress has been made throughout the world during a relatively few years of intensive research. Thus Endicott was able to say in 1957, "Just ten years ago, less than five per cent. of children with acute leukaemia lived as long as one year. To-day, the one-year survival rate has been raised to 50 per cent. by the use of chemicals and adjuvent therapy."

The screening of chemical compounds for anti-tumour activity requires a biological test system or, better, a spectrum of such systems. One cannot reasonably expect the results of experiments to surpass the limitations imposed on them by the test system used, and a heavy responsibility rests on those who are concerned with the biology of neoplasia, for it is they who must advise on the biological aspects of cancer chemotherapy.

It is common clinical experience that a neoplastic disease such as a leukemia will respond to a drug by a remission. Unfortunately, this remission is only temporary, and after a while the disease, no longer held in check and now resistant to the action of the drug, reappears and kills the host.

The development of resistance by leukaemic cells of the mouse to folic acid antagonists has been investigated by Law (1952). He considered that the development of resistance was not due to mutation, induced by the drug, of some of the leukaemic cells, but to pre-existing variant cells which, surviving the treatment killing the rest of the leukaemic cell population, proliferated to give a neoplasm resistant to further treatment by the drug.

The development of drug resistance has been described in a solid tumour also by Jackson (1954); the tumour being the Walker tumour of rats, and the drug triethylene melamine. Jackson considered that the growth of a drug resistant tumour after a latent period following a course of treatment with triethylene melamine must be due to the survival of a small number of tumour cells naturally resistant to the drug. He did not discount a possible mutagenic effect of triethylene melamine on the tumour cells, but thought that this was a less likely explanation.

Mammalian somatic cells reproduce by mitotic division, a process which normally gives rise to a genetically identical population. The mass of a tumour is produced by multiplication of the malignant cells, and it might therefore be expected that the members of the resulting tumour cell population would be similarly identical. That this is not so is strongly suggested by the evidence of Law and Jackson supported by the clinical course of leukaemia treated by chemotherapy.

In recent years, a number of investigators have examined tumours not as individuals but as populations of neoplastic cells. They have found that the cell populations of tumours are not homogeneous but heterogeneous ; containing many cell variants identifiable by their appearance. These various types of cell live together in a dynamic equilibrium which may be altered by changes in the environment with subsequent selective change in the make-up of the tumour as a whole.

It has been appreciated for many years that the cells of a malignant tumour may differ from one another in size and in general appearance (pleomorphism) and that abnormal mitotic divisions are frequently to be seen, but it was not until experimental tumours could be grown under controlled laboratory conditions in the ascites form, that is as free cell suspensions in ascites fluid within the peritoneal cavity of the host, that an adequate test system was available for the experimental analysis of chromosome numbers and morphology.

The chromosome complement of tumour cells in division has been examined by many workers, and it has been established that the cells of a given tumour show a wide variation in their chromosome numbers. If these numbers are plotted on a frequency distribution graph, two main classes of tumour are found ; those in which the most frequent chromosome number (the mode) is at or about the diploid number (forty in the mouse) and those in which the modal number is at or about the tetraploid number (eighty in the mouse). In addition to the cells at the mode, there is wide scattering of chromosome numbers on either side, and in a tetraploid tumour there may be cells with chromosome numbers from below the diploid number up to many hundreds.

Hauschka and Levan (1953) studying a spectrum of sixteen transplantable tumours of the mouse, found that those with a modal diploid constitution were invariably strain specific in their transplantation requirements, being lethal only to mice of the strain in which they originally arose, while those with a near tetraploid constitution showed varying degrees of indifference to hosts of other genetic constitutions, being lethal to mice of one or more foreign strains as well as to mice of the strain of origin.

In 1953 Makino and Kano working with certain ascites tumours of the rat found that each of the tumours studied contained within its cell population one or more strains of tumour cells, having characteristic chromosome constitutions, which remained unaltered in chromosome individuality throughout successive transplant generations. These cells were capable

of regular mitosis and were the primary contributors to the growth of the tumour.

In the same year Hauschka, on the basis of experiments involving the inoculation of single tumour cells into the peritoneal cavity of mice, strongly supported the concept of stem cell lines within tumour cell populations, and in 1955 Makino and Kano presented further evidence in favour of the stem cell concept. They used the Hirosaki sarcoma of rats, chromosome analysis of which showed a well-defined subdiploid mode, within which could be distinguished cells bearing one, two, three and four large V-shaped chromosomes, the other chromosomes of the cells being either rod or J-shaped. These large V-shaped chromosomes are absent from normal rat tissues. These modal cells were found to be capable of regular mitosis and persisted throughout serial transplantation. After inoculation of single tumour cells into rats, four cell clones were obtained in fifty-one attempts, two being characterised by 3V type cells, and two by 2V type cells (the 2V and 3V cells were the commonest in the stock tumour). The clones maintained their 2V and 3V populations throughout serial passage. Later, one cell was taken from the 2V clone, and one cell from the 3V clone. Both cells were injected into the same rat, and the resulting tumour was found to contain two races of cells, in which the stem lines consisted of 2V and 3V type cells respectively.

Collateral evidence in favour of the stem cell concept comes from studies of nuclear DNA, notably from the important work of Richards, Walker and Deeley (1956) using a photometric technique on the DNA/Feulgen complex.

As Hauschka and co-workers (1956) have emphasised, diploid, strain specific tumours usually contain about five per cent. of near tetraploid cells, and their proportion tends to remain constant throughout prolonged serial passage. These authors have demonstrated, however, that under the continued selective pressure of an immunologically hostile environment the near-tetraploid cells can crowd out the predominant diploid cells, to produce a tetraploid tumour with only about ten per cent. of diploid cells, and further, that when the derived near-tetraploid subline is returned to its original environment, the minority of diploid cells will gain ascendancy over the tetraploids with the re-establishment of a diploid tumour. Thus, appropriate experimental alteration of the environment is, by a process of immunoselection, capable of altering the equilibrium of a mixed tumour cell population, with resulting ascendancy of one line of stem cells over another.

These examples have been chosen to demonstrate that the cells composing a tumour are not identical, but that a tumour cell population is heterogeneous, forming a complex chromosome mosaic. Within the mixed cell population are one or more lines of stem cells which are responsible for the main growth of the tumour, while outside the stem lines a variable number of genetically unbalanced cells are doomed to extinction in one or more cell generations. The whole population is in a

state of dynamic equilibrium, an equilibrium which may be altered by appropriate stimuli.

The phenomenon of tumour progression is a bane to patient and surgeon alike. Foulds (1951) has defined progression as the advancement of a tumour by irreversible qualitative change of one or more of its characters, and in the first of his two Imperial Cancer Research Fund lectures on aspects of this characteristic of tumours has suggested certain principles or rules by which tumour progression is governed. When a tumour progresses it is capable of doing something it could not do previously ; thus the appearance of increased rate of growth, invasiveness, dissemination and the development of lack of control by hormones are all examples of progression.

Another example of tumour progression is the development of the ability of a solid tumour to grow as a free-cell suspension in ascites fluid in the peritoneal cavity, and one particularly well suited to experimental analysis. Klein and Klein (1956) have investigated the mechanism of the gradual conversion of certain solid transplantable tumours of the mouse to the ascites form. In this class of tumour, a suspension of tumour cells from the solid subcutaneous graft (the SS form), injected into the peritoneal cavity of mice will not produce an ascites tumour in the first transfer generation, but if the resulting intraperitoneal growth is serially passaged through further intraperitoneal generations, an ascites tumour (the AA form) will eventually result.

As an example of tumour progression, Klein and Klein wished to determine whether the gradual transformation was due to physiological adaptation of the tumour cells to their new environment, or whether the mechanism was one of selection. To this end they carried out three main experiments :

1. They found that the change to the ascites (AA) form once achieved was stable and irreversible. If the derived ascites tumour cells were passaged for a number of generations subcutaneously (the AS form) in mice, on mincing the solid AS tumour and injecting mice intraperitoneally, an ascites tumour was formed immediately without training through a number of generations.

2. If the original (SS) solid tumour were serially injected intraperitoneally, twenty-three generations were required before an ascites tumour was formed, while if the same tumour were injected intraperitoneally, harvested from the peritoneal cavity and injected subcutaneously in the next generation, alternating intraperitoneal and subcutaneous injections, only thirteen generations were required to produce an ascites tumour.

3. They made artificial mixtures of cells from the original untrained solid tumour and from the derived ascites tumour and determined the number of intraperitoneal transplant generations required to produce an ascites tumour. If the proportion of ascites cells were 5 per cent. or less, an ascites tumour could not be obtained immediately, but only after a number of transfers. A high correlation was found between the number of transfers required and the logarithmic proportion of ascites cells in the mixture.

From these and other experiments they concluded that this form of tumour progression was not due to an adaptive process but to selection,

a small proportion of variant cells with discontinuously high survival and growth capacities in the peritoneal fluid remaining masked when the tumour was inoculated into the peritoneal cavity and that a certain number of selective-exudate transfers was necessary before they could attain a critical proportion in the population and become manifest by changing the characteristics of the tumour. They were not able to determine whether these variant cells had been present in the tumour at the beginning of their experiments, or whether they had appeared during the course of their experiments by a naturally occurring mutation, but Hauschka had in 1953 demonstrated increased virulence in two sublines of the Krebs 2 carcinoma produced after inoculation of one to four tumour cells into baby mice. He suggested that the cell types isolated in the low-dose inoculations had been held in check by other elements in the parental population, and in spite of their greater virulence had been unable to displace competitive variants.

Morphological criteria, then, are not the only means whereby cell classes may be discerned in the mixed cell population of a tumour. There are present in tumours cells of irreversible variant types which have potentialities of action not shared by the other cells. These potentialities may be held in check by other elements of the cell population, and may not become manifest until a selective process raises their proportion above a certain critical level.

In 1942 Caspersson and Santesson described two cell types in histological sections of human carcinomas; these they designated types A and B and described also intermediate forms. The A type cell was small, round, with little cytoplasm which contained a high concentration of RNA, and was found near blood vessels and infiltrating normal tissues, while the B type cell was large, with much cytoplasm which contained a low concentration of RNA and was found in situations away from blood vessels and near areas of necrosis.

Later Craigie (1954) working on the survival of the cells of rodent tumours after freezing and thawing described in the cell population of ascites tumours two types of cell similar in appearance and RNA content to those described by Caspersson and Santesson. These he named types α and β, and added a further category, the paramorph, a highly contracted spherical form normally derived from the α cell type. He demonstrated that the cell types were not fixed but labile, defined certain conditions under which cells of one type would change into another type, and showed that survival after freezing and thawing was dependent on the cell assuming the paramorphic state when it was resistant to freezing, all cells remaining in the α and β forms being killed.

Trevan and I thought on general principles that the cells of a solid tumour close to blood vessels should be living in an environment with a relatively high oxygen concentration and a relatively low carbon dioxide concentration, while those away from blood vessels should be in a relatively high concentration of carbon dioxide and a relatively low

concentration of oxygen. In addition, those cells which were away from blood vessels and near areas of necrosis should, again on general grounds, be living in a more acid medium than those close to blood vessels owing to the build-up of acid products of metabolism and cell disintegration. Thomlinson and Gray (1955) had calculated gradients of the partial pressure of oxygen in various parts of cylinders of malignant cells in cancer of the bronchus, and we determined therefore to study the reactions of the cells of ascites tumours of the mouse when subjected to different partial pressures of oxygen and carbon dioxide and pH values.

The ascites tumour cells were mounted as shallow hanging drop preparations in a Perspex chamber arranged to allow water-saturated gas to be passed over the surface of the drop, and the reactions of the cells were recorded by cinephotomicrography. On setting up an experiment, the ascites tumour cells at first appeared as spherical bodies with little apparent nuclear structure. At the periphery there was a thin rind of cytoplasm which at times showed waving movements. In a gas flow of either pure oxygen or pure nitrogen the cells did not change from this rounded form. With a gas flow of either oxygen with 5 per cent. carbon dioxide or nitrogen with 5 per cent. carbon dioxide, most but not all of the cells spread out on the glass as bipolar, multipolar or discoid forms. In these conditions they would sometimes orientate themselves one to another and showed contacts between cells of a type never seen between cells in the spherical form. The spread out cells showed more internal structure; vacuoles, granules and mitochondria could be seen in the cytoplasm and the position and size of the nucleus could be made out. The edge of the cytoplasm showed waving movements and active pinocytosis could frequently be observed.

If pure oxygen or pure nitrogen were substituted for a mixture of 5 per cent. carbon dioxide in either gas, the cells withdrew their processes and reverted to the spherical form in a few minutes, and, if not exposed to the more alkaline conditions for too long, would spread out again on the glass if the carbon dioxide were restored to the mixture.

We concluded that under the conditions of our experiments:

1. The change from α to β cell type is not dependent either on oxygen lack or on a high oxygen tension in the cellular environment.

2. The change from β to α cell type is similarly not dependent either on oxygen lack or on a high oxygen tension in the cellular environment.

3. The change from β to α cell type may be brought about and maintained in the majority of tumour cells by a partial pressure of carbon dioxide of 40mm. Hg. in the cellular environment.

4. If carbon dioxide is removed from the environment of a population of cells in the β form, the cells will, during a few minutes, change into the α form.

The change from one cell type to another may either be due to a specific action of carbon dioxide on the cells, or to a shift in the pH of the

intercellular medium consequent on its equilibration with a gas mixture containing carbon dioxide. Preliminary studies suggest that the change is due to pH shift, but further experiments are required before a decision is reached.

We believe that the results of these experiments strengthen the opinion, held by some workers, that the α and β cells of certain ascites tumours and the A and B cells of solid tumours are directly comparable. We do not know the significance of the ascites cells which are refractory to the α-β cell change in our experiments; one is tempted to think that they may be cells possessing metabolic qualities and perhaps potentialities of action not shared by the other cells, but this is pure speculation and not yet supported by any experimental evidence.

The concept of a tumour cell population containing a minority of cells of irreversible variant type which possess potentialities of action not shared by the other cells, is now extended by the demonstration of reversible changes in the tumour cells imposed on them by their environment; changes which not only affect their appearance, but also their range of activities.

It is common experience in other fields of medical research that therapeutic advances must await methodological advances for, as I said earlier, one cannot expect the results of experiments to surpass the limitations imposed on them by the test system used. All seem to be agreed that there is no ideal test system or combination of test systems available for the screening of compounds for anti-tumour activity; indeed, it is remarkable that so much progress has already been made by the experimental cancer chemotherapists using the test systems the biologists have so far been able to make available to them.

The recent trend away from the classical methods of histological pathology and cytology and towards distribution studies in terms of morphology, cellular activity and perhaps most recently, tumour biochemistry as exemplified by the work of Sylvén and Malmgren (1957) has already increased the sum of our knowledge of the biology of tumours. A strong case can now be made out for the intensification and extension of research into the variant cell types which compose tumours, for if their characterisation could be achieved and if their interactions and potentialities of action could be more completely understood, some of the outstanding problems of the behaviour of tumours might well be solved, and by the application of the new knowledge it is possible that rational test systems might become available for use in chemotherapeutic research.

REFERENCES

CASPERSSON, T., and SANTESSON, L. (1942) *Acta radiol.* (*Stockh.*), *Supp.* **46.**
CRAIGIE, J. (1954) *Advanc. Cancer Res.* **2,** 197.
ENDICOTT, K. M. (1957) *J. nat. Cancer Inst.* **19,** 275.
FOULDS, L. (1951) *Ann. Roy. Coll. Surg. Engl.* **9,** 93.
HAUSCHKA, T. S. (1953) *J. nat. Cancer Inst.* **14,** 723.
——————— KVEDAR, B. J., GRINNELL, S. T., and AMOS, D. B. (1956) *Ann. N.Y. Acad. Sci.* **63,** 683.

——————— and LEVAN, A. (1953) *Exp. Cell. Res.* **4,** 457.
JACKSON, H. (1954) *Brit. J. Cancer* **8,** 336.
KLEIN, G. and KLEIN, E. (1956) *Ann. N.Y. Acad. Sci.* **63,** 640.
LAW, L. W. (1952) *Nature* **169,** 628.
MAKINO, S. and KANO, K. (1953) *J. nat. Cancer Inst.* **13,** 1213.
——————— (1955) *J. nat. Cancer Inst.* **15,** 1165.
RICHARDS, B. M., WALKER, P. M. B., and DEELEY, E. M. (1956) *Ann. N.Y. Acad. Sci.* 63, 831.
ROBERTS, D. C., and TREVAN, D. J. (1957) *Ann. Rep. Imp. Cancer Res. Fund* **54,** 18.
SYLVÉN, B., and MALMGREN, H. (1957) *Acta radiol. (Stockh.) Supp.* **154.**
THOMLINSON, R. H., and GRAY, L. H. (1955) *Brit. J. Cancer* **9,** 539.

COLLEGE PUBLICATIONS

READERS ARE REMINDED that the following publications issued or sponsored by the College may be obtained from the Editorial Secretary, Royal College of Surgeons of England, Lincoln's Inn Fields, London, W.C.2.

Lives of the Fellows, 1930-1951. By the late Sir D'Arcy Power, K.B.E., F.R.C.S., Honorary Librarian, and continued by W. R. Le Fanu, M.A., Librarian. A single volume, bound in blue cloth, of 889 pages, containing the Lives of all Fellows known to have died between 1930 and 1951. £2 2s. 0d. post free.

A Record of the Years from 1901 *to* 1950. Edited by Sir Ernest Finch, M.D., M.S., F.R.C.S. A slim volume, illustrated, containing a brief history of the College between the centenary and the 150th anniversary of the foundation with lives of all the Presidents since 1900, written by special contributors from their personal knowledge. In red cloth 9s. post free or red paper covers 5s. 6d. post free.

John Hunter, a List of his Books. A short-title bibliography of all known editions of John Hunter's books, compiled by the Librarian. Printed at the Cambridge University Press, and bound in green cloth. 2s. 6d. post free.

A Guide to the Hunterian Museum (*Physiological Series*). This gives a brief account of the physiological section of John Hunter's museum, the scope, design and historical value of which is unique. 48 pp. 1s.

A Descriptive and Historical Catalogue of the Darwin Memorial at Down House. Charles Darwin and his family lived at Down House, near Orpington, Kent, for forty-two years and it was here that most of his scientific investigations were made, including his work on the Origin of Species, published in 1859. 33 pp. 1s.

The Portraiture of William Harvey. The Thomas Vicary Lecture for 1948 by Geoffrey Keynes, M.A., M.D., F.R.C.S. With a descriptive catalogue and 33 reproductions of the portraits. £1 5s. 0d.

**William Clift*. By Jessie Dobson, B.A., M.Sc., Anatomy Curator. A new biography, fully illustrated, of the first Conservator of the Museum at the College. Published by William Heinemann Medical Books Ltd. Bound in blue cloth; 144 pages with frontispiece portrait and 31 plates. 8s. 6d. post free.

**A separate cheque for this publication would be appreciated.*

THE COLLEGE TIE

THE DESIGN is a College crest (an eagle proper holding a mace of gold) repeated on a maroon background. The tie is made in pure silk or silk and rayon, and also available are squares in the same design and tubular scarves. These may be worn by the following: Fellows and Members of the College; Fellows and Licentiates in Dental Surgery; Fellows of the Faculty of Anaesthetists; holders of the special diplomas granted by the Royal Colleges through the Conjoint Board; postgraduate students attending educational courses at the College. The tie can be obtained from Messrs. T. M. Lewin & Sons Ltd., 1-3 Jermyn Street, St. James's, London, S.W.1.

IMPERIAL CANCER RESEARCH FUND

ON SUNDAY, 23rd November, the B.B.C.'s "Week's Good Cause" appeal was devoted to the Imperial Cancer Research Fund. The broadcast was given by Mr. A. Dickson Wright, M.S., F.R.C.S., the Honorary Treasurer of the Fund. The following is the text of his appeal :

"Good evening,—A lifetime as a surgeon has not taken away the hesitancy I always feel when I use the word cancer ; it is a disease so ruthless and poignant that to most normal people this must be so. It hovers over us like a black cloud wrecking happiness and hopes, and we yearn for the day when it will finally be brought to an end.

"The answer is research and still more research and therefore I ask your help for this, the pioneer institute of cancer research in the world. For fifty-six ever-growing years our workers have sought the answer and in their searches have found a reply to many a problem and have by their contributions lightened the burden and loosened the grip of the disease. In 1958 people's chances are fifty times better than when we started with the blessing of Edward the Seventh in 1902—and that is due to the practical application of research.

"We know that smoking and other pleasures carry a quota of the disease—a small one it is true—and we torture ourselves over giving up our simple pleasures to avoid the risk. But let us at least persevere with research and discover the basic cause so that these things will no longer be of any account—and we can live unafraid.

Mr. A. Dickson Wright during his broadcast.

"As a surgeon I tend to divide mankind into two classes ; those who have had an operation and those who have not. Listening to me must be many with a thankful heart for what has been done for them by surgery in the past and I estimate that in this land there are 300,000 who have escaped from the fell

clutches of this disease by surgery. Let them each send a gift of thanksgiving, and this appeal would be an automatic success.

"Others there are whose hearts are full of sorrow for those that they have lost, and they should help us so that others may not suffer in the same way.

"Finally, who is there who will not join the last joyful shout of 'Thank God' which will rise to heaven when this monster is finally laid low—and laid low he will be. How will he feel who enjoys this great discovery knowing that he has himself made no contribution to it ?

"I hope and trust that this discovery will come to this land, in which many a momentous discovery in medicine has been made. There was Jenner and smallpox, Ross and malaria, and Lister who brought the mercy of surgery by ending wound sepsis, and finally the whole vile concourse of septic disease including tuberculosis took flight when the magic finger of Fleming pointed the way.

"So rally to our help and take your place beside us in the fight against this disease. Take pen and write, take a note from your pocket book, or send me a postal order in the morning, to Dickson Wright, Imperial Cancer Research Fund, W.C.2."

Over 7,000 contributions have so far been received in response to this appeal from all quarters of the country and are continuing to come in. The final total cannot yet be stated but will exceed £12,000.

LETTERS OF JOHN HUNTER

THE COLLEGE LIBRARY has lately acquired two autograph letters of John Hunter, both hitherto unrecorded.

The first, obtained from Dr. Richard Hunter, M.R.C.P., is of particular interest. It is Hunter's application to a Governor of St. George's for his "vote and interest" in the election of a Surgeon to the Hospital in the vacancy caused by the death of Thomas Gataker. It is dated 20th November 1768, and, though written by a clerk, is signed and addressed by Hunter in his own hand. Hunter was duly elected. The letter has a fine red wax impression of a seal which appears to be a bust of William Harvey.

The second letter is an undated Consultation, probably from the later part of Hunter's life, addressed to "Mr. Crowfoot, Surgeon, Ipswich." It is entirely in Hunter's hand, and discusses a case of deafness: "How far the deafness arises from disease in the Membr. Tymp. I will not pretend to say, but it is probable it assists or at least should be attempted to be cured, and what will do so is not so clear. How far injecting in some astringent or how far sweet oil with a little of the ungt. citrinum would do I do not know . . . probably electricity might be of service. I wish I could say more but all those diseases are obscure."

GRANT OF FELLOWSHIP DIPLOMAS

AT THE RECENT Final Examination for the Fellowship four candidates out of fifteen were successful in Ophthalmology, seven candidates out of twenty-three in Otolaryngology, and ninety-two out of 321 in General Surgery.

At a meeting of the Council on 11th December 1958 Diplomas of Fellowship were granted to the following:

†DAWSON, David Andrew (*St. Bartholomew's*)
MYLES, John Graeme Boulton (*St. Bartholomew's*)
*FFOOKS, Oliver Owen Frazer (*St. Bartholomew's*)
†RANSOME, Joselen (*Royal Free*)
BALL, Michael Joseph (*King's College*)
BRYANT, Kenneth Marrable (*Charing Cross*)
ALTMAN, Barry (*Westminster*)
SHAW, Norman Edward (*Sheffield*)
†ROBERTSON, Malcolm Sleeman (*St. Mary's*)
SMITH, Joseph Colin (*University College*)
LOEFFLER, Frank Elias (*The London*)
WILSON, John Walker (*Glasgow*)
NAIDU, Maddimsetti Venkataswami (*Andhra*)
HARDY, Eric Gordon (*Aberdeen*)
ASIRVATHAM, Augustus Appadorai (*Madras*)
BEARE, Maurice Sydney (*Cork*)
*CHAUDHURI, Prosunendra Mohan (*Calcutta*)
KUMARASINHE, Merlyn (*Ceylon*)
MUKERJEE, Bijay Chandra (*Lucknow*)
ORAM, William John (*New Zealand*)
SEN, Sumitra (*Punjab*)
DAS, Sujit Kumar (*Calcutta*)
YADAVA, Deva Nandan Prasad (*Patna*)
FONHAM, Dennis Geoffrey (*University College*)
CHANMUGAM, Julian Ranjithan (*Ceylon*)
DUNSTONE, George Hargreaves (*Durham*)
KABRAJI, Dadi Kekhushru (*Bombay*)
MANDER, John (*University College*)
SEEVARATNAM, Samuel Jayam (*Ceylon*)
CHESTER, Brian Charles Michael (*Queensland*)
†NEAME, John Humphrey (*University College*)
PAREKH, Bipinchandra Ranchoddas (*Bombay*)
SHAH, Feroz (*Punjab*)
†SHAH, Pravinchandra Amrital (*Bombay*)
CASSON, Phillip Rayner (*Sydney*)
GILL, Devinder Singh (*Punjab*)
GRIMSDELL, David James (*Westminster*)
MORRIS, Edwin David (*Wales*)
PEARSON, John Roy (*Birmingham*)
*PIGOTT, Louis Joseph (*Queensland*)
YOUSSEF, Mahmoud Kamel Aly (*Cairo*)
ARMSTRONG, William Louther Hunter (*Melbourne*)
BIRBARA, George (*Sydney*)
*CHER, Ivan (*New Zealand*)
COLLYMORE, Henry Wesley Moulton (*St. Bartholomew's*)
HOBSLEY, Michael (*Middlesex*)
†ISMAIL, Hussein Kamel (*Cairo*)
LATHAM, Geoffrey Rourke Welsford (*Sydney*)
RYALL, Robert James (*Cork*)
WALKER, Geoffrey Fleetwood (*Middlesex*)
BANERJEE, Chinmoy (*Calcutta*)
BENNET, Edward Glin (*Dublin*)
HANCOCK, Dudley Owen (*Middlesex*)
HUCKSTEP, Ronald Lawrie (*Middlesex*)
JHAVERI, Vimla Bhogilal (*Delhi*)

GRANT OF FELLOWSHIP DIPLOMAS

LALLJEE, Nazimhusain Mohsinbhoy (*Bombay*)
MACLEISH, Donald Gordon (*Melbourne*)
NAYAR Balakrishnapillai Thanuvan (*Bombay*)
PEKERA, Wilfred Samuel Emmanuel (*Ceylon*)
PLUMLEY, Peter Francis (*Middlesex*)
ROLLO, Alexander John (*Melbourne*)
SALLIS, Julian Gerald (*Cape Town*)
SHARMA, Parmanand (*Agra*)
SHARER, William Copland (*New Zealand*)
WATTS, Harry George (*New Zealand*)
WOOD, Edwin Carlyle (*Melbourne*)
WOOLF, Cyril Isaac (*University College*)
ANAND, Sundaram Vivek (*Agra*)
BHANSALI, Shirish Kanchanlal (*Bombay*)
BOWER, David Bartlett (*St. Bartholomew's*)
CASTLE, John Lindsay (*Sydney*)
CULLUM, Victor John Leslie (*Witwatersrand*)
EL-SAYED, Hamdy Mahmoud (*Cairo*)
GREEN, Hymie (*Witwatersrand*)
JAMES, Vernon Cecil (*Witwatersrand*)
JARDINE, James Lewis (*New Zealand*)
KAPUR, Tilak Raj (*Osmania*)
LLEWELYN, Donald Manton (*Sydney*)
LYNCH, Peter Francis (*Liverpool*)
MANN, Arnold (*Melbourne*)
MEHTA, Sorab Jal (*Bombay*)
MUIR, John David Henry (*Melbourne*)
SRINIVASAN, Mahadevan (*Madras*)
TAKTAK, Samih Yousif (*Beirut*)
THOMAS, Harold (*New Zealand*)
ALIMUMAL, Abubakar Mohammad (*Bombay*)
BROWN, Maurice William (*Adelaide*)
CLEZY, John Kenneth Albert (*Adelaide*)
JOSHI, Manohar Janardan (*Bombay*)
KEMP, Richard Ernest (*Belfast*)
PATEL, Amritlal Rambhai (*Bombay*)
SHACKLETON, Michael Elliott (*New Zealand*)
†SHAHEEN, Omar Hassan (*Guy's*)
VORA, Laxmikant Naranji (*Bombay*)
BURKILL, Katharine Mary (*University College*)
COX, John Samuel Tweedale (*Adelaide*)
EHRLICH, Frederick (*Sydney*)
SUBRAMANIAN, Sambamurthy (*Bombay*)
VINNICOMBE, John (*St. Thomas's*)
VOHRA, Balbir Krishan (*Calcutta*)

* In Ophthalmology † In Otolaryngology.

SAYINGS OF THE GREAT

"Health is that state of mind in which the body is not consciously present to us; the state in which work is easy and duty not too great a trial; the state in which it is a joy to see, to think, to feel, to be."

Sir Andrew Clark (1829-1893)

"I do not want you to read these books because they are old but because they are good." *Advice to his students by Sir Norman Moore* (1847-1922).

Contributions are invited.

CENTENARY CELEBRATIONS OF THE ROYAL CHARTER INSTITUTING THE LICENCE IN DENTAL SURGERY

22nd, 23rd, 24th July 1959

IN JULY OF this year the College is celebrating the foundation of the Diploma of Licence in Dental Surgery which was established by Royal Charter on 8th September 1859. It may not be widely realised that by Section 48 of the Medical Act of 1858 it was made lawful, by Charter, for the Queen " to grant to the Royal College of Surgeons of England power to institute and hold examinations for the purpose of testing the fitness of persons to practise as dentists. . . ." This the Queen did, and the Charter of 8th September 1859 laid it down that the College " should have power to institute and hold examinations for the purpose of testing the fitness of such persons. . . ." The first examination was held in 1860 and the significance of this Charter is that the College did not require the new licentiates to be Members of the College and thereby created a separate dental profession.

It says much for the liberal principles of the College and the good sense and common interests of both professions that after one hundred years they are still so closely associated within these walls, although dentistry's long tutelage under the aegis of the General Medical Council came to an end two years ago in the establishment of an autonomous General Dental Council. There has, of course, been a separate British Dental Association for some eighty years, since Licentiates of the College are not eligible for membership of the British Medical Association unless they hold a medical qualification as well.

The College proposes to hold a Centenary Celebration on July 22nd, 23rd and 24th when the theme of the meeting will be the progress dentistry has made during the past hundred years. There will be scientific demonstrations by the dental schools of the United Kingdom. Professor Bradlaw will deliver the first Menzies Campbell Lecture and an historical exhibition will be set up. A symposium on the cleft palate has also been arranged to deal with the developmental, surgical, orthodontic and prosthetic aspects of the syndrome.

The Annual General Meeting of the Faculty will be enlivened by a Reception of delegates from overseas, there will be a Centenary Festival Dinner and a reception by the University of London. There will also be a special reception in the College for Licentiates whose own particular Centenary this is.

ANATOMICAL MUSEUM

THE SPECIAL DISPLAYS are temporarily discontinued owing to reorganization of the museum.

LIST OF " OBSERVABLES " DESCRIBED IN THE ANNALS JULY 1947—JUNE 1958

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APPOINTMENT OF FELLOWS AND MEMBERS TO CONSULTANT POSTS

K. OWEN, M.R.C.S., L.R.C.P., F.R.C.S.	Consultant Surgeon to St. Peter's, St. Paul's and St. Philip's Hospitals.
D. W. CLARK, M.B., B.S., F.F.A.R.C.S.	Consultant Anaesthetist for Thoracic and General Surgical Anaesthesia to The United Leeds Hospitals.
N. SLADE, F.R.C.S.	Consultant Urologist to Southmead Hospital Group.
J. W. DICKSON, M.B., B.S., F.R.C.S.	Consultant Orthopaedic Surgeon to Ipswich and East Suffolk Hospital Group.

The Editor is always glad to receive details of new appointments obtained by Fellows and Members, either through the Hospital Boards or direct.

DIARY FOR JANUARY

Thur.	22		Final F.F.A. Examination begins.
		5.00	PROF. J. W. DICKSON—Hunterian Lecture—Pathological ossification in nervous disease with special reference to traumatic paraplegia.*
Mon.	26		Basic Sciences Lectures and Demonstrations begin.
Tues.	27	5.00	DR. R. C. B. PUGH—Erasmus Wilson Demonstration—Problems in bladder pathology.*
Wed.	28		Primary F.R.C.S. Examination begins.
Thur.	29	5.00	PROF. J. S. CALNAN—Hunterian Lecture—The surgical treatment of speech disorders.*

DIARY FOR FEBRUARY

Tues.	3	5.00	MR. RODNEY SMITH—Arris and Gale Lecture—The anatomy and physiology of the bile and pancreatic ducts and their surgical significance.*
Wed.	4		D.O. Examination and Final L.D.S. Examination (Part I) begin.
Thur.	5	3.45	DR. R. MCP. LIVINGSTON—Arnott Demonstration—The human embryo. The development of form.*
		5.30	MR. VICTOR RIDDELL—Otolaryngology Lecture—Thyroid glands and recurrent laryngeal nerve.*
Fri.	6		Basic Sciences Lectures and Demonstrations for Dental Students end.
Mon.	9		Anaesthetic Course begins.
Tues.	10	3.45	DR. F. C. CHESTERMAN—Imperial Cancer Research Fund Lecture—Heterotransplantation of human tumours and tissues.*
Wed.	11		Final L.D.S. Examination (Part II) begins.
Thur.	12		D.Phys. Med. Examination (Part I) begins.
		2.00	Ordinary Council.
Mon.	16		HUNTERIAN FESTIVAL.
			Course in Clinical Surgery begins.
		4.00	SIR REGINALD WATSON-JONES—Hunterian Oration—Surgery is destined to the practice of medicine.*
			HUNTERIAN DINNER.
Tues.	17	5.00	DR. W. A. H. RUSHTON—Edridge Green Lecture—Visual pigments in the living eye of normal and colour-blind men.*
Thur.	19		D.M.R.D. Examination (Part I), D.M.R.T. Examination (Part I) and D. Phys. Med. Examination (Part II) begin.
		3.45	DR. A. HOWE—Arnott Demonstration.*
		5.00	PROF. A. SORSBY—Ophthalmology Lecture—Retinal aplasia: recessive and dominant forms.*
Fri.	20		Anaesthetic Course ends.
Tues.	24	5.00	DR. R. A. GOODBODY—Erasmus Wilson Demonstration.*
Wed.	25		Primary F.D.S. Examination and D.T.M. & H. Examination begin.
Thur.	26		D.M.R.D. Examination (Part II) begins.
		5.00	PROF. C. HAVARD—Hunterian Lecture—Non-malignant bile duct obstruction.*

* Not part of courses.

2

BILIARY OBSTRUCTION IN THE REGION OF THE PORTA HEPATIS

Hunterian Lecture delivered at the Royal College of Surgeons of England

on

13th February 1958*

by

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IN CLINICAL PRACTICE, cases of obstruction of the bile ducts in this particular region of anatomy are comparatively rare, though they are of acclaimed notoriety. In a series of 2,033 cases of disease of the gall-bladder and bile ducts treated in the United Birmingham Hospitals, there were ninety-three cases of primary obstruction in the region of the porta hepatis (4.5 per cent.).

When first encountering a case, one is assailed by personal lack of experience of such lesions and the knowledge which can be applied to provide a remedy or relief for the patients who are often afflicted at the dawn or in the prime of their lives, by lesions which are not always intrinsically fatal but which have fatal consequences in so far as they lead to the impairment of the drainage of bile with increasing liver damage. Unlike obstruction to blood vessels, no help is to be expected from the natural development of collaterals, and the surgeon is faced with relieving the obstruction or the eventual death of the patient. His task is made difficult, not only by the anatomical inaccessibility and the complexity and variations of bile ducts, hepatic artery and portal vein, but also by a characteristic inflammatory response to local extravasations of bile, varieties of cholangitis, and what is often misguidedly called " previous operative interference."

Types of lesion

Table I shows the different types of lesion that may be encountered and the incidence in this series. Cases of obstruction due to secondary deposits in the liver or in the hilar lymph nodes have not been included. One case of liver fluke, encountered on surgical travels, has been added ; also four cases of cholangitis from Mr. F. S. A. Doran.

Problems and experience in pathology

Besides the characteristics of each cause, there is also a general pattern or picture of the surgical pathology of the effects of obstruction on the bile ducts, the liver parenchyma and on liver function and bile formation.

* While the parish register of Long Calderwood, near Glasgow, says that John Hunter was born on the 13th February 1728, he himself observed the 14th as his birthday. Probably he was born during the night of 13th to 14th.

TABLE I

BILIARY OBSTRUCTION IN THE REGION OF THE PORTA HEPATIS

	Types of Lesion	
INTRAMURAL LESIONS	Neonatal	1
	Traumatic	1
	Inflammation	20+4
	Neoplastic	3
INTRALUMINAR OBSTRUCTIONS	Stone	2
	Foreign body	1
	Parasites	—+1
EXTRAMURAL LESIONS	Choledochal cysts	—
	Liver abscess	1
	Hydatid cyst	1
	Hepatoma and primary liver carcinoma	2
	Neoplastic hilar glands	*
	Secondary deposits in liver	*
	Renal swellings. Cysts	1
		93
	Total with additions=	98

* The number of cases of obstruction which is secondary to metastatic deposits in the liver or to infiltration of portal lymph nodes have not been included in the numbers of types of lesion.

With some special exceptions (fistulae) the clinical picture is one of jaundice, and the differential diagnosis between obstruction and primary liver disease must be considered, though the solution cannot always be found without exploratory laparotomy. The following discussion of special points in pathology is given in a manner to portray the problems as they are encountered by the surgeon at operation, at autopsy and in the surgical laboratory.

Neonatal cases and congenital causes

Different lesions and anomalies occur (Keith, 1933; Kirk, 1948; Gross, 1953; Bowden and Donohue, 1955). The commonest cause appears to be one of failure of canalisation of the endodermal bud, the "anlage" of the biliary tract, which grows out in the fourth to fifth week of life from the duodenum at the lower end of the foregut. The liver, which develops within the septum transversum from this bud, lies in close relationship to the duodenum, and it is only as the development of the foetus progresses that separation occurs, with elongation of the common and hepatic bile ducts and, incidentally, the formation of the gall-bladder. As a result of such elongation, stenosis and atresia may occur. It is also said that after primary canalisation, a period of occlusion from rapid endodermal proliferation takes place at about the fifth or sixth week (also occluding the duodenum). Normally restoration of the lumen follows, but, if not, partial or complete stenosis or atresia remains. Another variety of obliteration is fibrocystic disease in which there is an incomplete or atretic lumen (Fig. 1).

When congenital obliteration occurs, it may be generalised in the extrahepatic bile ducts or it may pick out the gall-bladder or any section

of the bile ducts in a bizarre fashion. If the gall-bladder is in continuity with the duodenum it will be found to be flaccid and empty save for some inspissated mucus. If the obliteration does not extend into the intrahepatic ducts, examination of the porta hepatis will reveal the left or right hepatic ducts bulging with pale or white bile, a relatively fortunate state of affairs if relief is to be obtained by a surgical by-pass. In some cases the bile

Fig. 1. Section of the bile ducts in a case of neonatal jaundice showing fibrocystic disease. The lumen (which contains inspissated mucus) was not in continuity with the duodenum. ×30.

ducts may be so small and empty as to make it extremely difficult at operation to distinguish between a failure of development and some of the hopeless forms of neonatal hepatitis and cirrhosis. In this respect the practical value of liver biopsy and frozen section is established, for where the liver structure is completely disorganised, fat and glycogen deposited, bile pigment granules and thrombi present with acute and chronic inflammatory cells, or bile ducts and canaliculi absent, the surgeon is quite unable to be of any assistance. There is some evidence to challenge the view that obliteration of the bile ducts is due to a fault in development, and to suggest that some cases are due to a stenosing cholangitis similar in nature to that affecting adults. Whether this disease spreads upwards from the duodenum or reaches the porta hepatis through the umbilicus and ligamentum teres or comes downwards from the liver is not known.

Case report

A girl aged thirteen days became jaundiced. Laparotomy revealed a flaccid gall-bladder. The bile ducts were tiny but patent and a fine probe passed into

Fig. 2(*a*). Cross section of part of the ligamentum teres showing a heavy infiltration of inflammatory cells. ×60

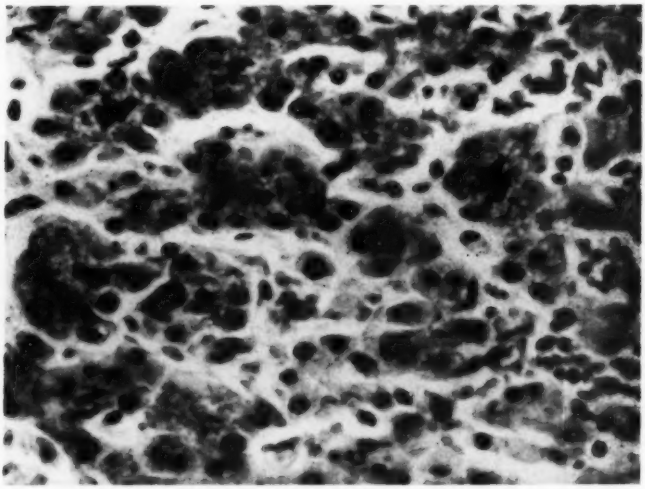


Fig. 2(*b*). A high power view of the liver parenchyma in the same case as Figure 2(*a*), showing bile pigment granules and thrombi consequent upon the compression of bile ducts by inflammatory cells. ×275

the hepatic ducts was " gripped " as by a stricture, and a diagnosis of intrahepatic obstruction was made, to be confirmed at autopsy. Histology of the liver showed compression of the bile ducts and a conspicuous infiltration of periportal spaces with lymphocytes and large mononuclear cells. Histology of the ligamentum teres revealed peri-arterial focal infiltration with lymphocytes and large mononuclear cells, and a similar heavy infiltration was found close to the remnant of the urachus (Fig. 2(*a*) and (*b*).)

In some cases of neonatal obstruction the jaundice is fluctuating and comparatively late in appearing (three weeks) which, with the appearances of intrahepatic periportal cirrhosis supports the idea of an acquired disease.

Of special interest is the report by Pappenheimer and others (1955) of the puzzling occurrence of neonatal jaundice due to the obliteration of the bile ducts in their stock of mice.

Other cases of obstruction are due to blockage of the smaller bile ducts with inspissated plugs of bile, while others are due to large bile thrombi caused by hyperbilirubinaemia in haemolytic disease of the newborn.

Strictures of traumatic origin

Almost all of these strictures develop in relation to a previous operation on the gall-bladder or the bile ducts, but very occasionally one will follow rupture of the liver. There is one case in this series in which the rupture extended into the porta hepatis and repair over a T-tube was successful in relieving the jaundice which had developed.

Damage to the bile ducts at operation, with resultant stricture formation is a subject concerning which a legion of contributions have been made (Cattell, 1947 ; Cole, 1948 ; Lahey and Pyrtek, 1950 ; Walters, 1953 ; Maingot, 1951 ; Ogilvie, 1957). Due in no small part to the stress laid in teaching and at examinations on the prophylaxis of such an accident, the incidence is very low, and in any collection of cases of obstruction at the porta hepatis, such lesions should not be expected to make up the bulk of the material. Of 1,730 cases having operations on the gall-bladder or common duct, eleven cases supposedly due to operative trauma occurred in the United Birmingham Hospitals (0.6 per cent.). An additional nine cases referred from other hospitals brings the total up to eighteen. Of these, sixteen (eight plus eight) were obstructions in the region of the porta hepatis. There is also a small group of cases, outside the scope of this paper, having low biliary strictures consequent upon disease or operations affecting the common bile duct in the region of the first and second parts of the duodenum (i.e., for duodenal ulcer).

Most cases of stricture following cholecystectomy can be ascribed to a deficiency in technique, such as : failure to dissect the cystic duct away from the hepatic duct ; failure to recognise common anatomical variations ; the imperfect dissection of and failure to obtain separate control of the cystic artery which leads to the haemorrhage resulting in blind and bulky seizure of bile duct and right hepatic artery in the jaws of forceps ; and an additional failure to realise that haemorrhage can be controlled by

thumb and finger pressure of the hepatic artery as it runs with bile duct and portal vein in the free margin of the gastrohepatic omentum (Seton Pringle's manoeuvre). Also a fundamental error in operative approach and technique is usually to be found in the inadequacy of the extent of the abdominal incision.

But there are other sides to the problem, for not all the cases of post-operative stricture can be said to follow damage by instruments. The sixteen cases presented here can be divided into two groups. In ten cases, obstructive jaundice followed closely upon the operation (within four or five days). In six cases the signs of obstruction were delayed for two or three weeks. The second group (late jaundice) suggests that either a slowly progressive lesion was set going by the operation, or the operation was performed in the presence of a pre-existing disease of the bile ducts. The slowly progressive lesion is, I believe, due to the effect that extravasated or pooled bile has upon the structures nearby, and the pre-existing disease is that condition or group of conditions labelled " stenosing or obliterative cholangitis."

The effect of extravasated bile

Bile which has escaped from the confines of its ducts is a powerful irritant to the tissues, a characteristic which is appreciated in cases of biliary peritonitis, when the patients are gravely if not fatally ill. The late effects of irritation are best seen when exploration of the subhepatic area is undertaken in cases where cholecystectomy, and particularly choledochotomy, have already been performed. The peritoneal cavity is often difficult to find, and the liver, stomach and colon may be found adhering strongly to each other. The first part of the duodenum shows a propensity to move upwards and adhere to the porta hepatis and here the fibrous tissue is thickest. The greater the number of operations performed upon the common duct, the tougher do these fibrous adhesions become, and each succeeding operation is more difficult and dangerous. There is no doubt that biliary strictures, once started, have a tendency to recur with an ever-increasing fibrous tissue reaction.

This phenomenon is also to be observed in the experimental animal. In the rabbit, with an intact biliary system, gall-bladder bile was aspirated and injected in a pool beneath the liver; six weeks later laparotomy revealed intense adhesions between the subhepatic aspect of the liver and the stomach and duodenum. If blood is allowed to pool instead of bile, no adhesions occur. Thirty-five per cent. Diodone did not produce the adhesions (this was done with a mind to the effects of pre- or post-operative cholangiography).

The reason for this irritant property of bile may be found through a study of the physico-chemical properties of the bile constituents, particularly the bile salts. Previous experiments (Rains and Crawford, 1953) have shown that bile salts have properties similar to the long-chain paraffin-salt detergents. The materials having properties of soaps and

Fig. 3. Cholangiogram through a T-tube fourteen days after choledochotomy had revealed a thickened, acutely inflamed common bile duct (" red-hot " duct). A constriction is to be seen at the confluence of the hepatic ducts.

detergents have long been used as sclerosants in the treatment of varicose veins. The introduction of bile salt solution, a soap solution or a detergent as pool into the peritoneal cavity of the rabbit did not, however, result in the typical adhesive response.

It is suggested that the excessive fibrous tissue response in the region of the porta hepatis following operations on the biliary tract, particularly where choledochotomy is performed, may be due to extravasated bile. Pooling and leaking of bile should be avoided and averted, and particular attention should be paid to the soundness of the ligature placed on the cystic duct in cholecystectomy, for this has been known to come off or to

be so imperfectly placed as to leak bile and so be responsible for subsequent stenosis of the bile duct. If a length of cystic duct is left behind (correctly, perhaps, through the force of pathological circumstance), a remaining or fresh stone will be the nidus of irritation which sets up an area of stenosing cholangitis where the common hepatic duct becomes the common bile duct. A sequestered stone in the right or left hepatic ducts will have the same effect.

Obstructions caused by inflammation

While stenosis occurs as a result of the fibrosis associated with extravasated bile (or sequestered stone), it also occurs as a result of what appears to be an internal infection of the mucous membrane and wall of the ducts—a stenosing cholangitis, which may be met with in an acute or chronic stage. In the acute stage the mucous membrane is acutely inflamed (a " red-hot " duct) and thus it is not surprising that in such cases cholecystectomy and choledochotomy should be followed by fibrosis and stenosis. Figure 3 shows a cholangiogram performed fourteen days post-operatively in a patient who had undergone cholecystectomy for chronic suppurative cholecystitis. One stone in the common bile duct necessitated choledochotomy and this revealed a thickened duct with an inflamed mucosa. The cholangiogram reveals a " neck " at the confluence of the hepatic ducts—a common site for localised stenosis. Other examples of the " red-hot " duct have been encountered.

In the subacute or chronic type, the sudden and perhaps symptomless appearance of unremitting jaundice in an otherwise healthy adult has a challenge of its own. From the clinical aspect the original diagnosis in

Fig. 4. Shows an exception to the " rule " that a flaccid gall-bladder is to be found in cases of obstruction at the porta hepatis. Carcinoma of the bile ducts involves the cystic duct, and a mucocoele of the gall-bladder has occurred.

such cases is often virus hepatitis, particularly where malaise and fever with abdominal discomfort are the commencing features. The diagnosis of hepatitis is questioned when the jaundice shows no sign of fading (in fact, increases in intensity) and the patient otherwise appears well. Liver function tests reveal definite evidence of obstruction, but little or equivocal indications of damage to the parenchyma. Obstruction of the common bile duct due to stone is a likely diagnosis, yet the absence of attacks of pain, fluctuating jaundice and fever demand second thoughts. Carcinoma of the head of pancreas is also a likely cause of the obstruction, though it is to be noted that the gall-bladder is not palpable. Exploratory laparotomy as a rule reveals an empty and flaccid gall-bladder, a sign or feature which, with some exceptions, is pathognomonic of obstruction of the hepatic ducts above the entrance of the cystic duct into the common bile duct. The exceptions are (*a*) where there is no gall-bladder, (*b*) when it is shrivelled by calculus cholecystitis and (*c*) where carcinoma has reached or arises in the cystic duct to cause a mucocoele (Fig. 4).

Extrahepatic stenosis

Examination of the region of the porta hepatis yields a variety of findings. The common hepatic duct alone or together with the common duct may be found to be of small, sometimes tiny, calibre. The wall may be of normal or of greatly increased thickness. Puckering of the fibro-fatty tissue around the transverse fissure with general obliteration of the normal anatomical features may occur. A distinct small hard nodule may be palpated with the fingers, or careful dissection upwards into the lips of the transverse fissure may reveal a small, firm, almost cartilaginous mass of tissue about 1cm. thick in the region of the juncture of the hepatic ducts. It is difficult to be sure whether such a nodule or thickening is inflammatory or neoplastic and histology will not always settle the issue (Figs. 5(*a*), (*b*) and (*c*)).

Above the obstruction, distended hepatic ducts may be encountered, but unfortunately not always so. In some cases the lesion appears to be intra- as well as extra-hepatic and to extend up the main and subsidiary ducts well into the substance of the liver (Figs. 6(*a*), (*b*) and (*c*)).

Intrahepatic stenosis

In other cases the firm nodule of tissue is absent, the ducts remaining a tiny calibre, being only able to accommodate a filiform bougie or ureteric catheter and gripping these instruments like any stricture. Such findings may be compared with those briefly recounted under " congenital" causes. There is, unhappily, yet another type of case in which the duct systems are narrowed yet no definite obstruction can be found. In one such case, after inconclusive findings at autopsy, histology of the liver showed fragmentation of the bile duct epithelium with disorganisation of the smaller ducts. Sections through the hepatic ducts showed necrosis, loss of the mucous membrane and extensive inflammatory changes in the subepithelium connective tissue. Aird (1957) refers to such obscure types

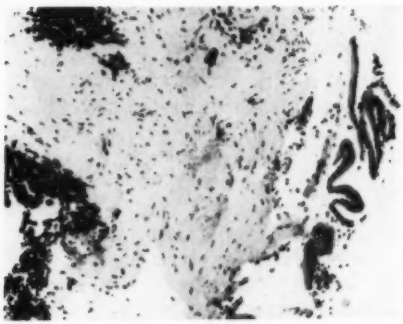


Fig. 5(*a*). Shows a section of an extrahepatic inflammatory nodule at the porta hepatis. ×120.

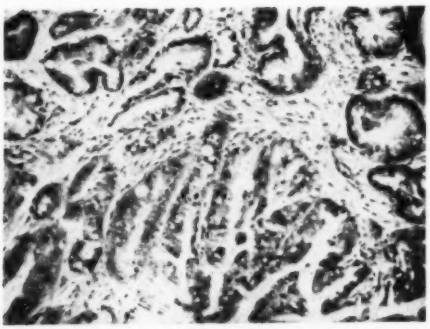


Fig. 5(*b*). Shows an extrahepatic nodule at the porta hepatis which is an adenocarcinoma. ×120.

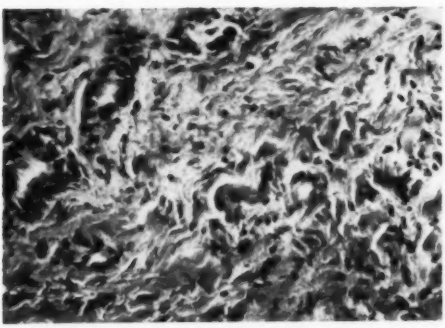


Fig. 5(*c*). The doubtful case. Section of an extrahepatic nodule at the porta hepatis showing extensive fibrosis, with a few areas of hyperchromatic cells in tubular formation. ×275.

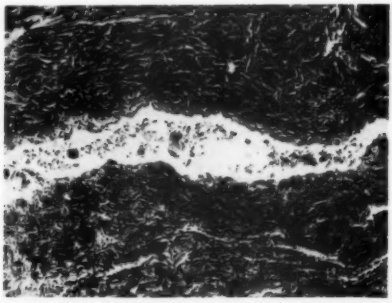


Fig. 6(*a*). Section of one of the main hepatic ducts showing massive fibrous tissue reaction which is strangling the lumen. Necrosis of the mucous membrane has occurred and a false lining has been laid down in places. (A characteristic of any stricture.) ×60.

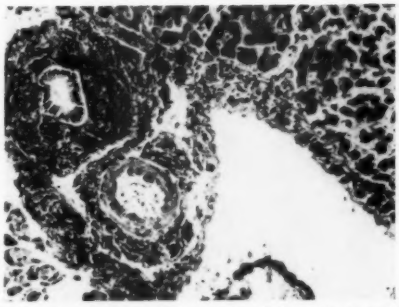


Fig. 6(*b*). Shows that the cholangitis has extended up the intrahepatic bile ducts. There is extensive periductal fibrosis. ×200.

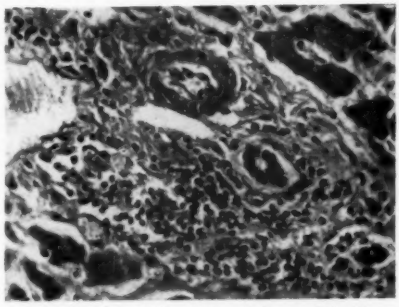


Fig. 6(*c*). Shows a fine bile channel in the periphery of the liver, surrounded with inflammatory cells which are advancing in front of the fibrosis which has ascended from the extrahepatic ducts. ×275.

of intrahepatic duct obstruction, particularly those in which a cholangiolitis or bile thrombi block the finer ducts. These patients (neonatal cases included) may linger, jaundiced, for a period during which the exceedingly high level of free cholesterol in the serum is manifest by xanthomata in skin folds as well as in internal organs.

The aetiology of this group of conditions is obscure. The variations in the site and the extent of the pathology suggest that there is no common cause. When the common bile duct is equally affected, especially where the whole mucous membrane is inflamed (the " red-hot " duct already mentioned) it is feasible to suggest regurgitation of bile and pancreatic secretion from the duodenal ampulla. Taking a comparison from the behaviour of the larvae of the liver fluke, which migrate up the common bile duct from the duodenum, motile bacteria should likewise have no difficulty. Unfortunately, attempts made to find bacterial infection have met with negative results, but this may be due to restriction of the range of culture media. Biochemical as well as bacteriological examination of the bile in cases of intrahepatic and extrahepatic cholangitis have not been

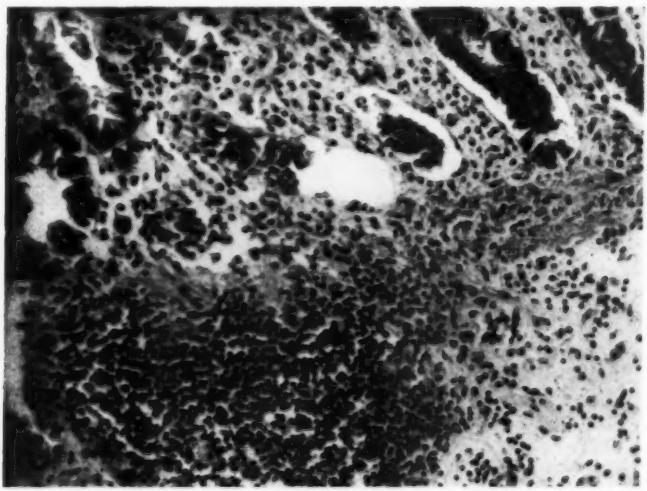


Fig. 7. A section of the mucous membrane of the ascending colon, showing one of the foci of non-specific inflammation occurring in a case of stenosing cholangitis.

helpful. According to Peyton Rous and McMaster (1931), because the gall-bladder is not in continuity, the bile is " white bile." Any alterations in constituents are the result of mechanical obstruction.

The general appearance of the liver is usually of little help, unless there is obvious cirrhosis. Usually the liver looks tense with a dark green hue from the peripheral collections of bile, but otherwise appears normal.

In two cases of stenosing cholangitis concomitant inflammatory changes have been noted in the bowel. In a case of intrahepatic obstruction a patchy non-specific inflammatory reaction was found in the ascending colon (Fig. 7). In a case of extrahepatic cholangitis there were appearances of ulcerative colitis on sigmoidoscopy. This is worth noting since Aird quotes two cases of Crohn's disease with proliferative fibrosis of the common bile duct.

Primary carcinoma

It has been stressed that a localised extrahepatic stenosis may not be due to an adeno-carcinoma (Figs. 5 (*a*), (*b*) and (*c*)). Carcinoma of the bile ducts does not show any tendency to remain localised for long for it spreads with great rapidity through the intrahepatic biliary tree, doubtless (like cholangitis) because of the rich plexus of lymphatics which surround the bile ducts. Carcinoma of the gall-bladder frequently spreads in this way. Of the thirty-five cases in this series, fourteen were of the gall-bladder, eighteen of the hepatic ducts and the remaining three were considered to have arisen in the cystic duct. Though cases of carcinoma of the gall-bladder not obstructing the porta were not included, the figures do suggest agreement with Willis that carcinoma of the bile ducts is just as common as carcinoma of the gall-bladder.

OBSTRUCTIONS DUE TO OTHER CAUSES

Stone

Stones lying in the hepatic ducts would most likely be the " remaining stone " following cholecystectomy and choledochotomy. One of the two cases encountered was considered to be due to this, being shown in the left hepatic duct by the post-operative cholangiogram. Since pre-operative cholangiography has been introduced there should be less likelihood of the " remaining stone " being a problem. In the other case (no previous operation) a solitary pigment stone was obstructing the left hepatic duct.

Parasites

Hydatid cysts. These cysts, when affecting the liver, can by position, size or number obstruct the main hepatic ducts by pressure from without. In one case a cyst involving the falciform ligament extended up into the porta hepatis and was compressing the hepatic ducts.

Liver fluke (Fasciola hepatica Linnaeus, 1758). This rare, well-remembered cause of biliary obstruction still occurs. The fluke lives in the biliary passages of a mammalian host (the herbivores—sheep, ox, goat, camel, elephant, horse, etc., with man as an alternative) producing a disease commonly referred to as " liver rot " (cystic enlargement of the bile ducts, adenomata of the biliary epithelium and periportal cirrhosis). A general toxaemia, cachexia and jaundice develops. Eosinophilia up to 54 per cent. has been recorded. Unusual foci of infection, such as the pharynx, lungs and brain may occur. The intermediate host is the appro-

Fig. 8(*a*). Shows a cholangiogram following reconstruction of the bile ducts round a T-tube.

Fig. 8(*b*). (Same case as in Figure 8(*a*).) Cholangiogram showing filling defects due to stone formation in the reconstructed bile ducts.

priate snail (lymnaea), which in a moist environment is actively penetrated by the miracidia which come from the large operculate eggs (approx. 140 × 80μ) passed with the faeces of the host. The miracidia eventually become cercarial larvae which emerge from the snail to swim about in the water, to encyst in the form of white spherules on swamp grasses and water plants (cress). The mammal consumes the grass and the larvae emerge from their cysts in the duodenum, to migrate up the common duct into the biliary passages where they settle down and mature into a flat and leaf-like worm (30 × 13mm.).

Other varieties of fluke and worm have been recorded (Aird, 1957).

Foreign bodies

Metal or plastic tubes used for reconstruction of the bile ducts are, of course, foreign bodies, and may be responsible for secondary stone formation, infection and an even greater degree of stenosis from fibrosis (Figs. 8(*a*) and (*b*).) In one case a length of ribbon gauze was found obstructing the common bile duct, extending with secondary stone formation upwards towards the porta hepatis. This gauze had been pushed down a biliary fistula by the patient herself who had undertaken her own dressings, and she had not noticed its disappearance within her when next she dressed it !

Freak cases of metallic foreign bodies, such as shrapnel, have been recorded.

PROBLEMS AND EXPERIENCE IN TREATMENT

The fundamental aim in the treatment of this syndrome is to overcome obstruction. In the few cases of simple intraluminar obstruction (such as stone, foreign body or parasite) the technique of removal is simple in comparison with those methods presently to be described. In most cases the intention of the surgeon will appear to be frustrated by fibrosis and inaccessibility when the exploration is made. The exact anatomical position of the obstruction has to be ascertained, as well as the nature of the pathology ; often a difficult task, for it has been shown that variations occur in every one of the main classifications of disease. An intrahepatic lesion cannot be by-passed, but one which is extrahepatic is usually amenable. A case of carcinoma of the bile ducts may not always be considered beyond the pale of surgical endeavour, especially since it has been shown that a diagnosis of this nature may be difficult in those cases where only a small nodule is found in the porta hepatis. Even when carcinoma is certain, the situation of the growth may be such as to make a palliative by-pass operation a safe and effective procedure, improving the quality of life by relief of jaundice, if not materially prolonging the patient's days.

Anatomy of the region

To enable the surgeon to obtain the maximum relief for his patients, an increased knowledge of the anatomy of the region is just as essential

as the understanding of the natural history of the lesions that are encountered. The parts requiring study are ; the transverse fissure, the quadrate lobe, and the hepatic artery and bile ducts.

The transverse fissure

Through this fissure the bile ducts, hepatic artery and portal vein emerge from or enter the liver. The position of the fissure in relation to the junction of the hepatic ducts affects both the surgeon's judgment and efforts as regards the feasibility of operative relief (Fig. 9). A " high "

Fig. 9. Diagram to show the variation in the position of the transverse fissure in relation to the confluence of the hepatic ducts.

position of the fissure, revealing lengths of right and left ducts, is obviously more promising than a " low " position. Another feature of the fissure is that it has margins, or lips, possessing varying degrees of mobility, and which are not integrated with the ducts and vessels ; for Glisson's capsule (like the pia of the brain) is continuous as a double sheath, extending into and returning from the substance of the liver. Any mobility of the margins of the fissure will facilitate retraction and so aid exposure, though quite often the nature of the pathology offsets this anatomical advantage by " freezing " the area with fibrous tissue or carcinoma.

The quadrate lobe

The quadrate lobe is not a kind of " no-man's land " or part of the right lobe of the liver : it is part of the true left lobe. In a useful monograph, Gans (1955) has confirmed previous work to show this, using vinylite injection techniques of hepatic artery, bile ducts, portal and hepatic veins (Figs. 10(*a*) and (*b*)). The edge of the quadrate lobe lies in juxtaposition to the anterior aspects of the right and left hepatic ducts. My personal understanding of this anatomy is that in this situation it is an " edge " of the liver, structurally peripheral rather than central, in spite of its actual position. Therefore a limited piecemeal resection can be undertaken without fear of encountering large vessels and this gives valuable exposure of those aspects of the ducts where most needed. On

Fig. 10(*a*). Vinylite cast of liver by injection of portal vein, showing anterior aspect and the division into right and left lobes, the quadrate lobe being a portion of the left lobe.

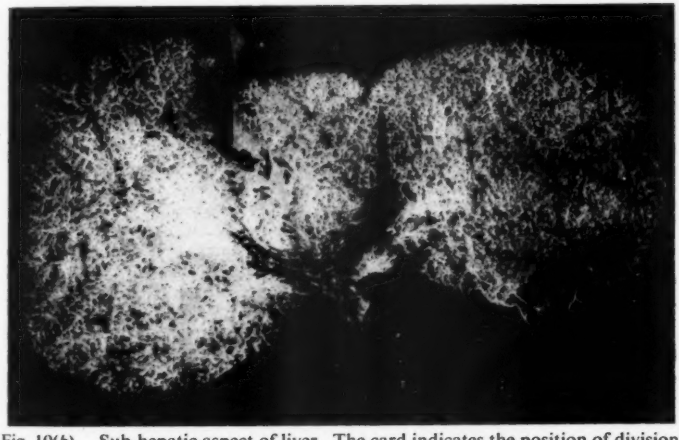


Fig. 10(*b*). Sub-hepatic aspect of liver. The card indicates the position of division between right and left lobes, and the black arrow the position of the gall-bladder fossa. It is a peripheral part of the quadrate lobe which abuts on to the porta hepatis.

dissecting into this area it is only when clearing the anterior aspect of the left duct that one has to be concerned with the position of the duct and artery of the quadrate lobe and, if necessary, their division, reconciled with the fact that no major duct or vessel has been destroyed.

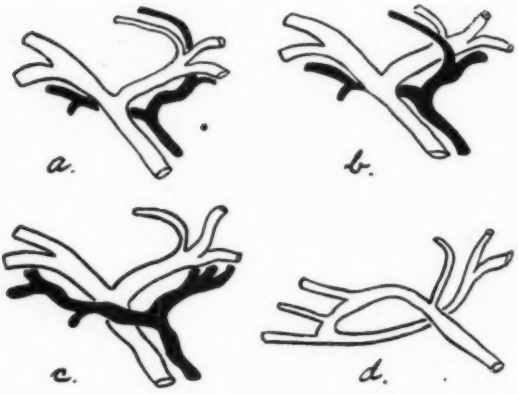


Fig. 11(*a*). The normal arrangement of major ducts and arteries, present without gross variation in 80 per cent.

Fig. 11(*b*). An artery to the quadrate lobe passes in front of the left hepatic duct.

Fig. 11(*c*). The right hepatic artery passes in front of the common hepatic duct.

Fig. 11(*d*). The left hepatic duct arises as a prolongation of the right duct which doubles back behind the common hepatic duct (4 per cent.).

The hepatic artery and the bile ducts

The normal relationships of the bile ducts, hepatic artery and portal vein are as well known as the fact that anomalies are frequent. One important relationship which is more or less constant and which is relevant to the problem of dissection, is that the bile ducts are nearly always the most ventrally placed structures when a cross-over occurs between duct and artery (in 86 per cent. of people). Figure 11(*a*) shows the normal arrangement of major ducts and arteries, one which is present without gross variation in over 80 per cent. of people. Figure 11(*b*) shows an anomaly of the artery to the quadrate lobe, passing in front of instead of behind the left hepatic duct. This has been personally encountered in one operation ; it is easily recognised as it is about 2mm. in diameter, and it can be divided if necessary. Figure 11(*c*) shows the right hepatic artery crossing in front of the common hepatic duct, an anomaly which is fortunately rare as it could be technically embarrassing (also encountered, Doran).

Concerning abnormalities in the arrangements of the bile ducts, one must expect to find that in many instances the left and right hepatic ducts are foreshortened or that some of the larger ducts come together to become the common hepatic duct at one point (Fig. 12). One rare (4 per cent.) variation of the left hepatic duct which would give concern

Fig. 12. A cholangiogram showing abnormality of hepatic ducts; several major ducts coming together at one point.

in location is where there is a prolongation of the right hepatic duct which doubles back in a circle to pass under the common hepatic duct (Fig. 11(*d*)).

Pre-operative measures

As in all cases of obstructive jaundice, attention should be paid to the deficiency of prothrombin in the blood, which occurs through failure to absorb the fat-soluble vitamin K (in one case the prothrombin was 24 per cent. of the normal control). Up to the last war, operations in cases of

jaundice were attended by a formidable mortality and it is fair to say that the pre-operative restoration of the prothrombin level by injections of vitamin K or its analogue (menaphthone B.P.) has played a major part in making this kind of surgery safer (Illingworth, 1939). The menaphthone is given intramuscularly in doses of 10 to 15 mgm. for four to seven days. Vitamin K_1 may be given intravenously, but a word of caution is necessary, for the coagulability of the blood is a finely adjusted characteristic and the intravenous injection may swing the pendulum so quickly as to swing it too far, with the resultant dangers of thrombosis.

Blood transfusion, which in the last fifteen years has become an integral part of the surgeon's armamentarium, is essential. The patients are always anaemic and pre-operative transfusion is necessary when the haemoglobin level is below 80 per cent.

Concerning diet, glucose is given for its calorific value as well as for its protein-sparing effect. It is doubtful whether essential amino-acids such as methionine or choline are specially indicated.

Liver function tests and urinalysis, which are part of the investigations, are of value in the determination of the timing of operation and with regard to premedication and anaesthesia. For example : if repeated tests show a persistence or an increase in the degree of obstruction and in parenchymal damage, operation must not be delayed. Gross impairment of function will result in a tendency for the patient to remain longer than usual under the influence of barbiturates, morphine and pethidine, and this is coupled with a definite, though variable, resistance to curarisation.

Incisions and approach

It is not easy to be dogmatic about the best incision. For greatest access, in the neonatal cases as in the adult, the thoraco-abdominal approach (of accepted value in porto-caval anastomosis) is superior to others because the diaphragm is also divided, making it possible to displace the liver into the pleural cavity and to rotate it so that the subhepatic aspect and the porta hepatis look upwards at the surgeon (Fig. 13(*a*)).

It is usual to make the abdominal part of the incision first, to confirm the pathology or to free adhesions or trace a fistulous track. In many cases, however, a paramedian incision will have been made, on the reasonable assumption of a simpler and commoner diagnosis. This being so, it is important to remember that adequate exposure is vital and that the incision must be extended. From the upper end of the wound a fresh incision can turn laterally, along the line of the eighth rib or interspace, so that with division of the costal margin and costal resection or intercostal incision the chest can be opened, the diaphragm divided and the liver displaced. A similar conversion with a more acute turning angle can be made with a subcostal incision (Holman, 1950).

In some instances the surgeon may be averse to this kind of exposure. I find that a fairly suitable alternative can be obtained by extending the lower end of the paramedian incision in an arc outwards into the loin

(Fig. 13(*b*)). This is a muscle cutting extension, which heals well, and it allows a large flap of the right upper portion of the abdominal wall to be turned upwards and so give the necessary exposure. In cases of fistula or where extensive subhepatic adhesions are to be expected, the approach

(*a*)

Fig. 13(*a*). The thoraco-abdominal approach.

(*b*)

Fig. 13(*b*). The curved abdominal approach.

is particularly useful, and under such circumstances the incision is commenced in the flank and the abdomen opened well away from the site of fibrosis.

It would be invidious to make these incisions eponymous. Several names could be applied to each variety.

Findings and dissection

This section is divided into three parts :

1. When the patient has not previously been operated on ;
2. when the patient has previously been operated on ;
3. dissection into the porta hepatis.

(1) *When the patient has not previously been operated on*, the abdomen is opened and a well ordered examination conducted. The flaccid gall-bladder (with exceptions) has already been alluded to, but its importance as a sign in this variety of obstruction is worth accentuation. Examination of the porta hepatis and the common bile and hepatic ducts will reveal one of the variety of lesions that have been described (carcinoma ; stenosing cholangitis—acute or chronic—localised or diffuse ; stone ; foreign body ; etc.). Cholangiography on the operating table, using the cystic or common bile duct is helpful in showing patency of the lumen

and the sites of obstruction. Sounding, using Clutton's steel sound, is another aide, the instruments being introduced through an opening made in the common bile ducts between stay sutures and, after observing the state of the wall and mucosa, they are passed downwards into the duodenum and upwards to the obstruction. The duct is often of small calibre and a fine sound is necessary to locate and assess the type of stricture that involves a length of right and left hepatic ducts (Fig. 14 inset).

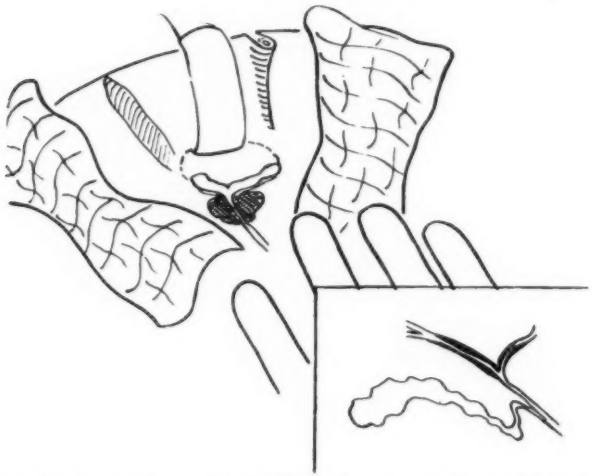


Fig. 14. Diagram to show aids to dissection (retractor, mops and hand) and the area of the quadrate lobe into which exposure is extended. The position of the nodule which may be found is indicated. *Inset.* Diagram showing flaccid gall-bladder and stricture of the hepatic ducts.

(2) *When the patient has previously been operated on.* Having entered the abdomen away from the site of disease it is necessary to embark on the tedious business of dissecting the adherent viscera away from each other. It is a good rule to identify the transverse colon and the liver first. These, with the omentum, and the stomach on the left, must be freed, gradually displacing the colon downwards. When the stomach has been identified this is used to trace out and mobilise the duodenum which will be found stuck with thick adhesions to the porta hepatis. If a fistula is present, an elliptical incision will have been made in the skin around the opening and the track followed down into the dense area of fibrous tissue. Using the sound as a guide the ducts are reached after the duodenum has been mobilised.

(3) *Dissection into the porta hepatis.* The aforegoing accounts can be continued together at this juncture.

In many cases it is difficult to find any trace of the common bile duct and gradual dissection upwards towards the transverse fissure must proceed

in the hope that a bulging stump or "nubbin" (Gross, 1953) of the dilated hepatic ducts will be found. A syringe and needle may be used for trial aspiration to localise the ducts, and in this respect one must stress that only a small syringe is necessary and that if bile is found, little if any should be withdrawn for empty and collapsed ducts are elusive. The purpose of Figure 14 is to demonstrate other aides to dissection as well as to show the area of the quadrate lobe into which the exposure is extended. Different liver retractors (without flanged blades which cut into the liver) are found necessary to retract the anterior lip of the transverse fissure and the quadrate lobe. The hand of the surgeon or assistant is important in maintaining the structures on the stretch to aid dissection. As in cholecystectomy the positioning of abdominal mops to pack off the stomach, the colon and the right paracolic gutter is essential. The surgeon may find that his best position is to stand on the left hand side of the patient, a position which I personally find most helpful, for the major ducts are in the line of vision as one looks directly into the porta hepatis.

As the dissection opens up the ducts, and a gratifying flow of white bile occurs, a succession of stay sutures is put in to mark their course. Fibrous tissue or neoplasm are removed piecemeal and, when required, that "edge" of the quadrate lobe which abuts onto the ducts. The anatomical variations which have been described (Fig. 11) are circumvented, or accepted and dealt with as they are met (possible division of the artery to the quadrate lobe). It is often impossible to visualise clearly the hepatic artery, but its position can be identified by touch.

The choice of relieving procedures

The techniques which are aimed to relieve biliary obstruction in this region are considered under the following headings:

1. Resection of a stricture with varieties of end-to-end anastomosis, including the use of indwelling tubes.
2. By-pass of the obstruction or restoration of biliary flow using the stomach, duodenum, jejunum (not Roux-en-Y) or gall-bladder.
3. By-pass of the obstruction using the Roux-en-Y type of jejunostomy.
4. Other procedures (bouginage, hepaticodochostomy, jejunal implant, etc.)

(1) *Resection of a stricture and varieties of end-to-end anastomosis* are techniques which can be altered to suit a particular case, being most feasible when the stricture is localised. When the common hepatic duct at its formation is involved, it is often necessary to sew the right and the left ducts side by side in a double-barrelled manner and then to divide the "party" wall to make the two small openings into one large one and then join this, with interrupted sutures, to the main duct below (Lahey and Pyrtex, 1950). Some kind of a tube is always necessary, serving two purposes; first to act as a splint and secondly to act as an efficient drain. From what has already been said about the effects of

extravasated bile in producing or enhancing fibrosis, it is to be expected that such an anastomosis will leak some bile unless it be adequately drained. In the undrained case such leakage or seepage is enhanced by the exhibition of the usual pain relieving drugs such as morphine or pethidine, since both of them cause a spasm of the sphincter of Oddi and produce a rise in biliary tension. Bile, through the "flowing" characteristic of its mucoid state, has an extraordinary propensity for leaking in long and almost never-ending strings from the smallest pinhole ; a phenomenon which is observed in cases of obscure biliary peritonitis when perforation of the gall-bladder is extremely difficult to find.

Indwelling tubes, whether metal, rubber or plastic, may be left *in situ*. The objections to such a tube are (*a*) that if it is retained indefinitely it is a nidus for infection, ulceration and stone formation (Fig. 8*b*) and (*b*) that if passed within three or four weeks of the reconstruction, the suture line, still in an active phase of repair, will stenose. If a tubular scaffold is to satisfy the demands which are made on it, it must be capable of remaining in position for at least two to three months so that maximum fibrosis and shrinkage will have already taken place round it before removal is effected. Thus T-tubes, with one long arm of the T on one side to be passed into the duodenum, are necessary. The other arm of the T, around which the ducts are reconstructed, is trimmed to a suitable length and "guttered" by removal of a segment of the circumference as the surgeon desires. It is important to remember (and this is stressed by Lahey) that the long external drainage rim of the T-tube should not be introduced into the ducts at the site of the suture line for this will surely encourage further stenosis when reaction occurs following the removal of the tube : the tube should be put in through an opening in the common bile duct below the line of anastomosis. For reconstruction where the left and the right hepatic ducts are separately involved, the upper arm of the T-tube may be split to provide splintage for each duct, though a specially manufactured Y extension is preferred (Lahey and Pyrtex, 1950).

While this seems to be a reasonable method for reconstructions and has been accorded a good measure of success it is not always so. Biliary mud and stones may form with rapidity, which cannot be dispersed by flushing out the tube or by employing the recognised gall stone "solvents" (Rains, 1951) (Figs. 8*a* and *b*). Infection with any obstruction causes rigors and chronic ill health and this may occur after the tube has been removed in an apparently successful case. According to Lahey, excellent or good results were obtained in 73 per cent. of cases in which end-to-end anastomosis was performed. In extremely localised strictures using a simple Mickulicz type of plastic operation (/ to —) he has recorded 100 per cent. success. On the other hand Cattell (1947), also with great experience, was inclined to the view that the longer these cases are followed the more the recurrence of symptoms of obstruction will be

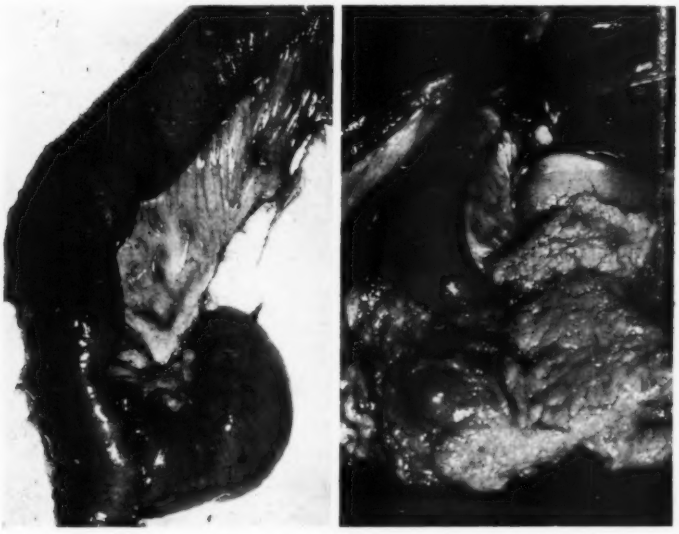
noted. At that time, in thirty cases of using a vitallium tube for reconstruction a satisfactory result was obtained in nineteen. However, Cattell feels that the most satisfactory results follow end-to-end repair of the duct over a T-tube with subsequent removal of the tube.

(2) *Reconstruction or by-pass using stomach, duodenum or jejunal (not Roux) loop.* To say that these methods of anastomosis lead to stenosis with subsequent cholangitis may appear to be a sweeping statement, but it is not far from the truth. Although Lahey and Walters claim a high percentage of success, 75 to 80 per cent. when choledochoduodenostomy is performed, the percentage falls to about 50 per cent. after hepatodochoduodenostomy. This variety of anastomosis may fail through the excitation of fibrous tissue reaction caused by the movements of the duodenum which tend to elongate the anastomosis and perhaps narrow it (Maingot, 1951). It is more probable that the stenosis that occurs is due to irritation caused by regurgitation of gastro-duodenal contents, and on this account surgeons have aimed at a stoma which is as wide as possible, to allow for the narrowing which will naturally follow the operation. However, such a large opening, while not stenosing readily, allows the free passage of food and gastro-intestinal juices up the ducts (demonstrable by barium meal studies), which may lead to cholangitis and cholangiolitis. Aird compares the cholangitis from regurgitation to oesophagitis from regurgitation—with subsequent stricture formation. It may be argued that there is a place for a carefully constructed opening which is small, not allowing regurgitation, and therefore free from cholangitis with subsequent fibrosis. Personally I do not think that this view can be upheld, believing that stenosis is just as inevitable. Heavy infection of the bile with rigors is, of course, due to stenosis (*cf.* urethral stricture). The varieties of choledocho- or hepaticodochoduodenostomy or enterostomy are many (Grey Turner, 1955 ; Lahey and Pyrtex, 1950 ; Walters, 1953).

If the gall-bladder, cystic duct and common bile duct are free from disease, the gall-bladder could be used to by-pass the obstruction. I have no personal experience of this method, but believe that the difficulties concerning end-to-end reconstruction of the ducts will still apply (more so since one has to take into account the concentrating powers of that viscus).

(3) *By-pass using the Roux-en-Y (The Roux Loop) type of jejunostomy.* This valuable technical manoeuvre was described by Dr. Roux in 1907. For a recent helpful exposition of technique (concerning oesophageal replacement) that of Allison should be referred to or, for wider interest, that of Yudin (though in Russian, the illustrations speak for themselves). The isolated limb of the Roux loop of jejunum is the drain *par excellence;* always, by virtue of the direction of peristalsis, draining onwards into the lower jejunum and ileum, yet not obstructing the passage and free mixing of gastro-duodenal secretions and contents. Regurgitation of food or secretions up this isolated loop is limited, and it has been shown by

Warren Cole (1948) that lengths of over twelve inches ensure that regurgitation will not encroach near the upper end (Fig. 15*a*). It would



(*a*) (*b*)

Fig. 15(*a*). The Roux loop. Fig. 15(*b*). The Roux loop has been brought up behind the colon and in front of the duodenum. The retractors are being withdrawn and the liver allowed to fall back into place to cover the loop.

appear to be the most satisfactory form of by-pass in this type of case, and in practice this has been found to be so. Allen and Warren Cole are in some respects the pioneers of the application of the Roux-Y operation to the problems of stricture of the bile ducts. In a series of sixty-three operations Cole obtained a successful result in 78 per cent.

My particular contribution towards the usage of the Roux loop in these high biliary obstructions concerns the size of the aperture required for anastomosis into the porta hepatis. If regurgitation can be avoided by the use of a long loop, a large aperture can be safely aimed at, for the objection to the size of anastomosis when using stomach or duodenum does not apply. One should avoid cutting right across any duct, for when the fibrosis of the normal process of repair occurs the opening may stenose to a pinhole size. The ducts should be opened up widely and made into gutters, if necessary by removing strips of their anterior or more superficially placed walls (Fig. 16). In this way, when the fibrosis of repair occurs, it will be linear along a much greater circumference.

The open end of the Roux loop is not sewn to the open ends of the ducts but is planted over and around them like a sucker-foot and so effecting the widest aperture of anastomosis possible. Figure 16 also shows the

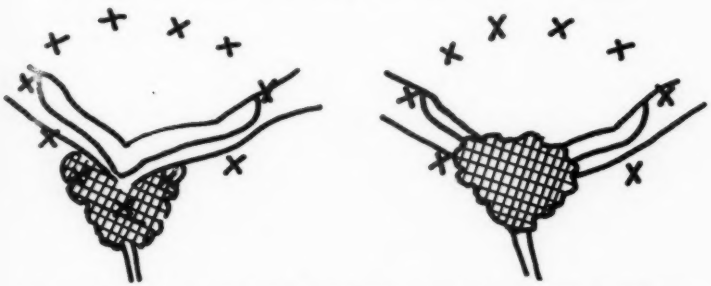


Fig. 16. Showing two positions of obstructing nodules in the porta hepatis, the guttering of the ducts and the position of the sutures used to plant the upper end of the Roux loop around the openings.

approximate positions of the interrupted sutures which are used to unite the seromuscular layer of the bowel with the fibrous tissue in the porta hepatis. The posterior layer of sutures are placed first and then the bowel is pushed up into the porta hepatis and the sutures are tied (the knots are kept on the outside). The anterior layer is sewn to the edge of the excavated quadrate lobe. Some of these sutures may not retain their hold in the liver, but this does not give rise to concern, because when the liver is allowed to rotate back into its normal position the mass of the quadrate lobe covers up the Roux loop quite adequately (Fig. 15*b*). Extra sutures are placed where necessary to hitch the loop up into the liver and to offset any tension. Before the wound is closed a corrugated drain is inserted through a separate incision down to the site of anastomosis to the liver. Up to the present I have used this method eight times, the first case being done seven years ago.

Other procedures

In the cases where stenosis extends upwards in the walls of the main ducts of the liver (Fig. 14 inset) any form of by-pass operation as described in the last two paragraphs is out of the question. With severe narrowing of the ducts, in which filiform bougies are " gripped," drainage may be possible by employing ureteric catheters (Fig. 17). These may be brought out through or beside a small sized T-tube. If no common duct exists, a temporary hepatodochostomy should be aimed at, so that after the free flow of bile has been established, a Roux loop can be brought up as a second stage and sewn over the stoma in the porta hepatis. Cortisone may be used to delay or inhibit the inflammatory response if dilatation with bougies and indwelling catheters have to be used (*cf.* urethral strictures). I have used it on three occasions starting seven days post-operatively and continuing for six weeks (Figs. 17 and 18). If the gall-bladder appears normal it should not be removed in these cases.

Other varieties of hepaticodochostomy have been devised. In a recent case, where there appeared to be no hope of achieving a by-pass in the

porta hepatis, a large dilated duct was found close to the surface of the liver. Warren Cole has suggested that by using an exploring needle such large ducts may be found within the substance of the liver in such hopeless

Fig. 17. Localised intrahepatic cholangitis—the ureteric catheters which have been used to cannulate the strictures of the right and left hepatic ducts may be seen; also the flaccid gall-bladder. The cholangiogram is virtually normal, the ducts and the duodenum being well filled. Cortisone had been given to this patient, who has remained in good health since (three years).

cases. and that the Roux loop can be implanted in the liver to the requisite depth. Longmire's operation consists of a partial left hepatectomy with preservation of the left hepatic duct so that this may be implanted into the jejunum. This would be satisfactory if there were continuity between the right and left ducts at the porta ; but if this is so the operation seems

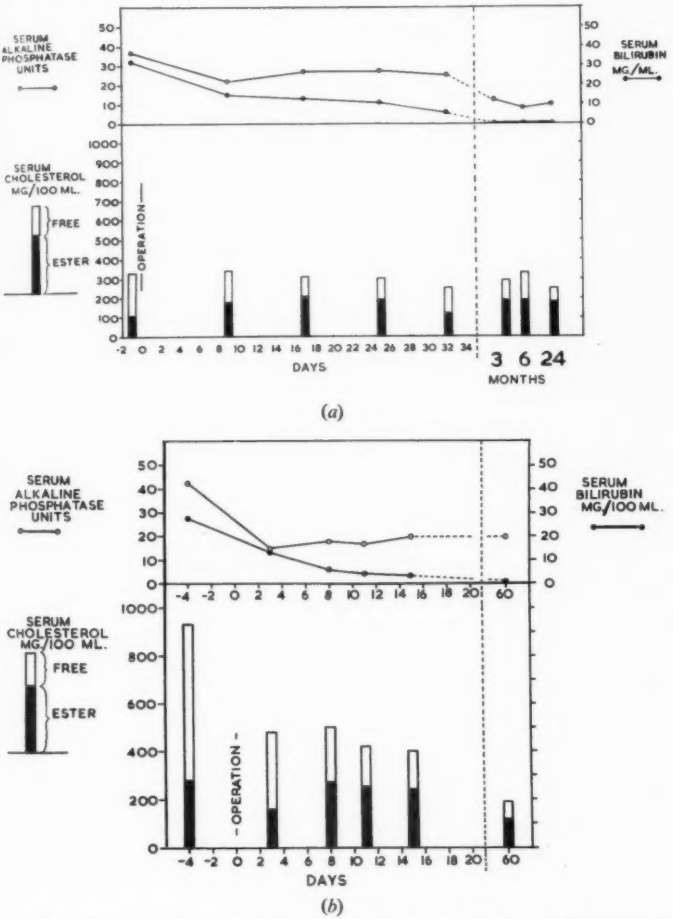


Fig. 18. Graphs showing the improvement in the serum alkaline phosphatase, bilirubin and cholesterol levels after relief of obstruction. The ratio of free to ester-cholesterol also returns to normal. Graph (*a*) is from a patient suffering from stenosing cholangitis treated by bouginage, ureteric catheterisation and cortisone. Graph (*b*) is from a patient in whom a carcinoma of the common hepatic duct was by-passed with a Roux loop.

unnecessary. In view of the anatomical division into the two main lobes it is doubtful if the right lobe can drain through its peripheral juncture with the left.

Post-operative problems

Post-operative progress may be as swift as after any gastro-intestinal operation (Fig. 18). Blood or blood-stained bile will seep through the drain, which may be removed about the fourth day. Any leakage of bile ceases by about the seventh day.

Antibiotics are not given as a routine; it may be false reasoning to suppose that their administration will diminish the inflammatory response in the porta hepatis or around any reconstruction, for some of the greatest fibrous tissue responses have been known to follow the sterilization of infection with antibiotics (the "penicillin" tumour in breast or hernia infections). Antibiotics such as chloramphenical or tetracycline must be considered where there is a degree of liver damage.

In addition to maintaining a correct water balance, care must be taken to watch for electrolyte imbalance. Patients who are draining bile to the exterior sometimes slip into extensive negative sodium balance. Estimation of the serum electrolyte levels will indicate the need for the administration of the requisite amount of sodium chloride or sodium lactate.

If cortisone is used as an ancillary to delay or modify inflammation and repair, the surgeon should be aware of the risks. Immediate dangers are; gastro-intestinal haemorrhage; leakage of the entero-enterostomy if a Roux loop has been performed, or in the other by-pass operations; and a diminished resistance to infections—particularly the "hospital staphylococcus." Future danger lurks in the tendency towards severe hypotension following subsequent operations; requiring control with further cortisone and even intravenous hydrocortisone (Slaney and Brooke, 1957).

Operations and results in the series

The form of presentation of this paper was designed with the intention of giving to the reader information on the natural history of the diseases and a commentary on the reasoning which governs the type of surgery to be adopted.

Table II has been constructed to provide a picture of the distribution of the different kinds of operations that have been employed in this series for the adult cases. The cases date from 1951. There is a discrepancy between the number of cases and the number of operations which is due to repeated operations in some instances.

Because the series (particularly of post-traumatic strictures) is small in comparison with those of Walters, Lahey and Cattell, it has been possible to indicate success, failure or death following the treatment of each case of benign stricture.

In malignant disease cure was never obtained, though satisfactory periods of palliation (up to eight months) have been achieved. There seems no point in giving a figure for mortality.

TABLE II

BILIARY OBSTRUCTION IN THE REGION OF THE PORTA HEPATIS. STENOSIS IN ADULTS. OPERATIONS AND RESULTS.

Type of Case	Laparotomy and closure or simple T-tube drainage	Reconstruction using tubes	By-pass (e.g., Hepatodocho-duodenostomy)	Roux loop	Other methods: Bouginage, Hepato-dochostomy, etc.	No. of operations	Deaths
Post traumatic .. 17 cases	NIL	11 × × 1 11 + × 9	+ × 1 × 1 × 111 9	111 111 6	NIL	24	2
Stenosing cholangitis 24 cases	1 × 111 × 1 + 11 + 11	1111 4	+1 2	11 2	(lc)(lc)11 (lc) + (+lc) + 8	27	6
Carcinoma .. .. 35 cases	25	3	1	4	4	37	*
No. of operations ..	36	16	12	12	12	88	

KEY: 1 = Successful cases × = Unsuccessful cases
+ = Deaths (lc) = Cortisone used
* = See text.

While the series in itself cannot provide irrefutable results, increasing experience with these diseases in this anatomical situation and the improvement in technique holds out good prospects in most non-malignant conditions, and sometimes a suitable quality of palliation in malignancy.

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REFERENCES

AIRD, I. (1957) *A companion in surgical studies.* Edinburgh, Livingstone, p. 1003.
ALLEN, A. W. (1945) *Ann. Surg.* **121,** 412.
ALLISON, P. R., and DA SILVA, L. T. (1953) *Brit. J. Surg.* **41,** 173.
BOWDEN, D. H., and DONOHUE, W. L. (1955) *Amer. J. med. Sci.* **230,** 305.
CATTELL, R. B. (1947) *J. Amer. med. Ass.* **134,** 235.
COLE, W. H. (1948) *Ann. Roy. Coll. Surg. Engl.* **3,** 111.
DICKSON WRIGHT, A. (1951) *Proc. Roy. Soc. Med.* **44,** 1010.
FAUST, E. C. (1930) *Human helminthology.* London. Kimpton.
GANS, H. (1955) *Introduction to hepatic surgery.* Amsterdam and London, Elsevier.
GRAY, H. K. (1951) *Proc. Roy. Soc. Med.* **44,** 1005.
GREY TURNER, G. (1955) *Modern operative surgery,* 4th edition. London, Cassell **1,** 907
GROSS, R. E. (1953) *The surgery of infancy and childhood.* Philadelphia, Saunders.
HEPP, J. (1957) *Utilisation du canal hépatique gauche dans les réparations diliaire difficiles.* A communication at the joint meeting of the Royal College of Surgeons with the Académie de Chirurgie de Paris. London, 30th May 1957.
HOLMAN, E. (1950) *Amer. J. Surg.* **90,** 464.

HULTÉN, O. (1938) *Hygiea (Stockh.)* **100,** 188.
ILLINGWORTH, C. F. W. (1939) *Edinb. med. J.* **46,** 762.
KEITH, A. (1933) *Human embryology and morphology.* 3rd edition. London, Arnold.
KIRK, J. (1948) *Ann. Roy. Coll. Surg. Engl.* **3,** 132.
LAHEY, F. H., and PYRTEK, L. J. (1950) *Surg. Gynec. Obstet.* **91,** 25.
LONGMIRE, W. P., and SANFORD, M. C. (1948) *Surgery* **24,** 264.
LOVE, R. J. McN. (1952) *Brit. J. Surg.* **40,** 214.
MAINGOT, R. (1951) *Ann. Roy. Coll. Surg. Engl.* **10,** 97.
OGILVIE, H. (1957) *Ann. Roy. Coll. Surg. Engl.* **21,** 319.
PAPPENHEIMER, A. M., CHEEVER, F. S., and SALK, H. (1955) *J. exp. Med.* **101,** 119.
RAINS, A. J. H. (1951) *Brit. J. Surg.* **39,** 37.
——— and CRAWFORD, N. (1953) *Nature* **171,** 829.
ROUS, P., and MCMASTER, P. D. (1921) *J. exp. Med.* **34,** 75.
SLANEY, G., and BROOKE, B. N. (1957) *Lancet* **1,** 1167.
SÖDERLUND, G. (1953) *Acta. chir. Scand.* **106,** 77.
WALTERS, W. (1953) *Ann. Surg.* **138,** 609.
WELLS, C. A. (1951) *Proc. Roy. Soc. Med.* **44,** 1011.
WILLIS, R. A. (1948) *Pathology of tumours.* London, Butterworth.
YUDIN, S. S. (1954) *Reparative surgery for impassable oesophagus* (in Russian). Moscow, State medical literature publications.

PROCEEDINGS OF THE COUNCIL IN JANUARY

AT A MEETING of the Council on 8th January, with Professor Sir James Paterson Ross, President, in the Chair, Sir Walter Mercer was appointed Robert Jones Lecturer for 1959. Mr. H. R. Thompson was appointed Thomas Vicary Lecturer for 1959.

Dr. R. F. Woolmer, F.F.A.R.C.S., was appointed the first British Oxygen Professor of Anaesthesia.

The award of the Joseph Clover Lectureship to Dr. H. J. Brennan was announced.

One diploma of Fellowship was granted.

The following diplomas were granted, jointly with the Royal College of Physicians : *Laryngology and Otology* (21), *Anaesthetics* (112), *Medical Radio-Diagnosis* (44), *Medical Radiotherapy* (15), *Psychological Medicine* (46), *Pathology* (6), *Public Health* (14), *Tropical Medicine and Hygiene* (4), *Child Health* (2).

The following hospitals were recognised under paragraph 23 of the Fellowship Regulations.

HOSPITALS	POSTS RECOGNISED		
	General (all 6 mths. unless otherwise stated)	Casualty	Unspecified
WORCESTER—Royal Infirmary and Ronkswood Hospital (Additional)	Regr. (12 mths.)		
ALTON—General Hospital (Redesignation)	*Redesignation* as H.S. as Regr.		
BIRMINGHAM—Dudley Road Hospital (Additional)	3 Pre-Reg. H.S.s		

INTRAVITAL TECHNIQUES FOR THE DEMONSTRATION OF LYMPHATICS

The introduction to an Hunterian Lecture on The Lymphatics of the Breast delivered at the Royal College of Surgeons of England

on

28th May, 1957

by

R. T. Turner-Warwick, M.A., B.Sc., D.M. (Oxon)., F.R.C.S., M.R.C.P.
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NORMAL PERIPHERAL LYMPHATICS are exceedingly thin walled vessels which, when empty, are virtually indistinguishable from the surrounding tissue. Under natural circumstances they can only be recognised with certainty during an operation when they are distended with lymph on the peripheral side of an occlusion ; fine fibrous cords are sometimes demonstrated as lymphatics but these are more often pathological remnants, if indeed they are lymphatics at all.

Chyle-containing lacteals were first seen and recognised as important by Aselius in 1622 ; the peripheral lymphatics were discovered as a result of further intravital observations in animals by Rudbeck and by Bartholin about 1650.

The accepted anatomical descriptions of regional lymphatics are, in most cases, the result of normograde post-mortem injections. A peripheral lymphatic can be located by distension with lymph or oedema fluid (Cruikshank, 1786 ; Mascagni, 1787) and injected directly with mercury (Nuck, 1697), prussian blue (Gerota, 1896) or Thorotrast (Gray, 1938). The proximal lymphatic trunks can be conveniently demonstrated by direct injection into a lymph node. Trunk lymphatics are competently valved and retrograde injection is not normally possible ; Sappey attempted to destroy the valves by partial putrefaction, but such methods inevitably lead to artefact.

These post-mortem techniques provide only a limited demonstration of lymphatics. The only intravital method that has been widely used is the spread of carcinoma, but this is dependent upon many other factors and only in the early stages (Handley and Thackray, 1954) is it of any value as a method of determining the regional lymphatic drainage.

Kinmonth (1954) has recently introduced a method of studying limb lymphatics in the patient. A peripheral lymphatic trunk is exposed and located by means of a distal injection of a diffusible dye ; diodone is injected directly into it to provide contrast for lymphangiography. This method has important clinical applications.

Certain regional lymphatics, such as those of the breast, do not lend themselves to direct injection because of the difficulty of locating the deeper vessels for direct injection. In order to study these, intravital methods must be used.

The regional distribution of lymph drainage can only be accurately assessed by tracing dyes and markers as they are transported by the

natural flow of lymph from an injection site to the regional nodes. Several methods have been devised for this.

Techniques

The injection is made directly into the tissue; the material is then removed, according to its nature, by vascular and lymphatic absorption. Most diffusible dyes are largely removed by the blood stream, but colour the lymph inasmuch as the tissue fluid is stained; particulate substances and those with a molecular weight in excess of about 20,000 are normally absorbed by the lymphatic system.

If regional drainage is being studied a single injection site is used and if tumour is present the injection should be made some distance from it.

The rate and volume of lymph flow varies greatly in different parts of the body, lymph from the stomach reaches the regional nodes in a few minutes, lymph from a resting limb takes considerably longer: it may take several hours before a recognisable concentration of dye injected into a non-lactating breast reaches the regional nodes.

Hyalase

The rate of lymphatic flow can be greatly increased by the addition of hyalase to the injection; this causes marked local oedema at the site of injection and increases the lymph flow to such an extent that exposed trunk lymphatics can often be identified simply as a result of distension by the flow of clear lymph. This method is very helpful in the intravital demonstration of lymphatics, but hyalase must not be used in the presence of malignant disease because of the increased risk of tumour dissemination.

(1) Diffusible dyes

Diffusible dyes have long been used for the intravital demonstration of lymphatics and provide good visual demonstration during operation; if they are to be used for clinical work they must be wholly eliminated from the body within a few days without residual local or general skin staining.

The colour of an intradermal injection of Patent blue and Evans blue will fade within a week. An intramammary injection of one ml. of a 3 per cent. solution rendered isotonic often provides adequate demonstration of local lymphatics and reduces to a minimum the transient, post-absorption, body blueness which results if larger amounts are used and the site of injection is not excised at operation.

The lymphatics in a specimen are demonstrated by direct and trans-illumination after rendering the tissues transparent by clearing. The whole specimen is dehydrated in the usual way with successive changes of alcohols; Benzine is a toxic chemical but is better for clearing large specimens than xylol because the result is less " yellow." Methyl salicylate or cedar wood oil is used for storage and viewing.

Unfortunately Patent blue and Evans blue tend to diffuse out of lymphatics during the dehydration of large specimens.

Pontamine Sky blue and Direct Sky blue are much more persistent diffusible dyes and stain the lymphatics which transport them so that they may be seen in the cleared specimen ; these dyes are similarly persistent *in vivo* and it is unwise to inject them into patients unless the site of injection is definitely to be excised before the dye can be generally absorbed.

(2) Particulate dyes

Particulate dyes such as Indian ink and colloidal graphite are absorbed by lymphatics less readily than diffusible dyes and naturally produce a permanent stain at the site of injection. They are not usually suitable, therefore, for the clinical demonstration of lymph vessels, but they may be useful for assessing the extent of mechanical spread along the tissue planes.

(3) Radio-opaque media

Thorotrast, a colloidal preparation of thorium dioxide, is a good medium for the direct or indirect post-mortem injection of lymphatics (Gray, 1938). Its colloidal nature facilitates entry into lymphatics and it is precipitated during fixation of the specimen so that it does not subsequently diffuse. Indirect post-mortem injection is, however, only irregularly successful in the breast where the local lymphatics are not numerous ; this can be greatly improved by injecting the specimen at the oedematous site of a recent pre-operative hyalase injection when this has not been contraindicated by local malignant disease.

Thorotrast can be demonstrated radiologically, histologically and in cleared specimens (by transverse illumination). It is, however, not of great value for intravital work because only a small proportion is removed from the injection site and this becomes too diluted with lymph during the process to provide adequate contrast in the vessels for lymphangiography of the specimen; these vessels can however be shown by passive filling with concentrated thorotrast as a result of massage of the injection site.

Thorotrast is an undesirable substance for clinical work because it is radio-active, it emits α-rays and has an extremely long half life. Interstitial injection regularly results in a local chronic foreign body reaction with progressive local fibrosis. Similar injections in rats produce a local fibrosarcoma (Selbie, 1938), but local malignant change does not apparently occur in humans ; there are, however, occasional reports of sarcoma and marrow depression which have been attributed to large intravascular injections many years previously (for angiography or hepatosplenography). While it is not always possible to be certain that thorotrast was responsible for these systemic effects the evidence is sufficient to contraindicate its clinical use for inessential purposes.

In the study of lymphatics there may be considerable value in assessing the extent of non-lymphatic local spread of an injection radiologically, for instance in about 10 per cent. of random intramammary injections, the medium enters the milk duct system and this may confuse the result

if it is not recognised. Dionosil, a particulate diodone used for bronchography can be used instead of thorotrast ; it behaves as a coarsely particulate substance with no special tendency to enter lymphatics.

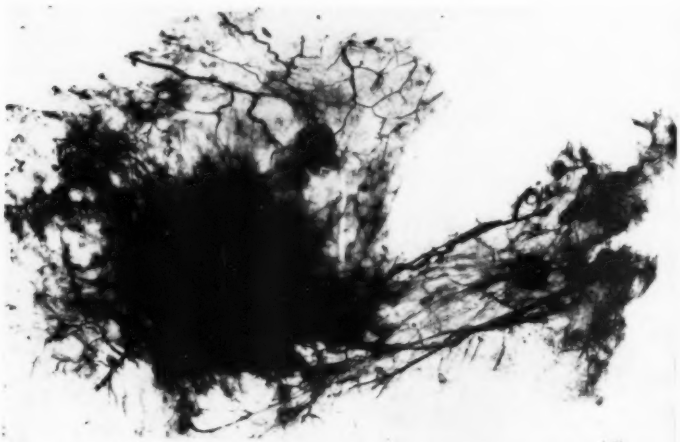

Fig. 1a. Lymphatics of Breast. Iron prussian blue method. Cleared mastectomy specimen viewed by transillumination. A=site of iron injection. B=Prussian blue in main axillary lymphatics. C=axillary lymph nodes. D=axillary blood vessels. E=internal mammary branches. F=lateral perforating branches of fourth and fifth intercostal vessels with paramammary lymph nodes. G=carcinoma.

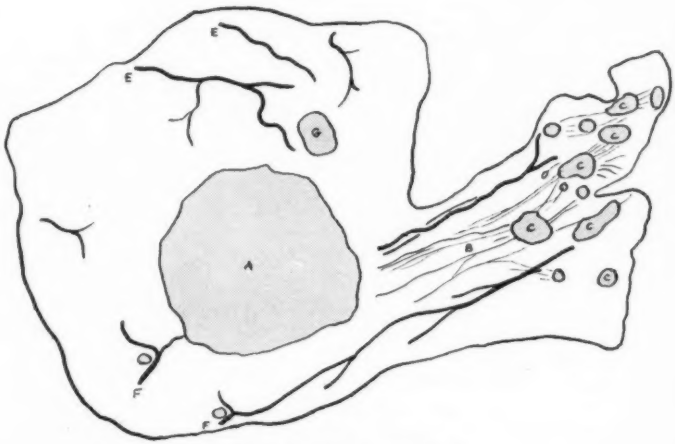

Fig. 1b. Diagram explaining 1a.

(4) Developing dyes

None of the substances available has approached the ideal for intravital demonstration of lymphatics in a specimen. Theoretically this would be a non-toxic diffusible substance of a relatively high molecular weight (which would ensure lymphatic absorption); colourless (to prevent skin staining over the injection); harmless and non-toxic (so that the site of injection would not have to be excised): once in lymphatics it should be possible to precipitate it into a particulate colour which would remain in the lymphatics during mass clearing of the specimen.

In search of such a method various iron containing compounds were tried including iron dextran (Imferon) and iron saccharate. These are not colourless, but their uptake by lymphatics is fair and they can be precipitated as prussian blue at the site of injection, in the lymphatics and in the lymph nodes, by fixation of the specimen in acid-potassium-ferrocyanide-formalin (Turner-Warwick, 1955).

This method is simple in theory but its technique is complicated. Iron preparations vary in their *in vitro* Prussian blue reaction, this seems to improve after injection into the tissues. Glass dishes and Japanned copper entymological pins avoid contamination with iron. The exact composition of the fixing fluid can be varied to suit the situation, Formol saline containing 0.5 per cent. potassium ferrocyanide and 0.5 per cent. potassium ferricyanide gives fair results. Acidification with acetic acid may be preferable to hydrochloric acid because the fluid does not become spontaneously blue so rapidly; the solution is however unstable and it must be freshly made and changed every day. The specimen can be protected from blue deposit by wrapping in a single layer of lint. The penetration of the developing fluid is poor and accessibility to the bulky specimen must be increased by suitable incisions, especially when there is a large area of skin covering. It is particularly important to wash the specimen thoroughly before transfer to the dehydration alcohols in order to prevent uniform blue staining; it can then be cleared in the usual way.

Although this method has yet to be perfected, it has provided some useful demonstrations of regional lymphatic trunks in cleared specimens (Fig. 1). It cannot be used as a reliable method for assessing the regional lymph node drainage because the reticulo-endothelial system of the lymph node tends to pick up endogenous iron from haemolysis in bruises or local inflammatory lesions. In earlier studies injected iron was distinguished by using a special batch of Imferon supplied by Messrs. Bengers containing radioactive iron Fe 59.

(5) Radioactive tracer methods

The most valuable method of assessing regional lymph drainage is radioactive colloidal gold Au 198. In its colloidal form the gold precipitates on the tissue proteins on interstitial injection. About 90 per cent. is precipitated on fixed tissue proteins and is retained at the site of injection, the remaining 10 per cent. is attached to mobile proteins (or taken up by

macrophages) and because the molecular weight of these proteins exceeds 20,000 they are naturally absorbed almost entirely by lymphatics. Much of the gold is retained by the reticulo-endothelial system of the lymph node ; incidentally the proportion of the original dose that reaches and is

Fig. 2. Autoradiograph of mastectomy specimen. 300 microcuries of radioactive colloidal gold Au 198 injected into lower outer quadrant (*a*) six hours before mastectomy. Fourteen axillary lymph nodes (*b*) show radioactive pickup. The film has been exposed by the radioactive areas and a soft tissue X-ray has been superimposed.

retained by the lymph node is far too small for this to be a practical method of treating carcinoma quite apart from the fact that tumour areas in lymph nodes do not pick up the gold. The general body absorption and, therefore, the background count is extremely small.

Bloom and Gregory (1953) tried this method for studying breast lymphatics using a scintillation counter ; they found that the radioactive scatter of the primary injection site overshadowed the relatively small uptake in the nearby lymph nodes, but the method was more useful in the limb where the injection site could be further away. Hultborn *et al.*, (1955)

used a scintillation counter after excision of the site of injection by radical mastectomy.

In the present investigation the regional node activity has been assessed by autoradiography of the thin dissected specimen in addition to counting methods. Scintilographic methods can be used for measurement both in the specimen and in the patient.

The most economical method is to receive 50 millicuries of colloidal Au 198 in one ml ; this can be diluted during its early life to give an injection dose of 50 to 250 microcuries. The half life is 2·7 days and, therefore,

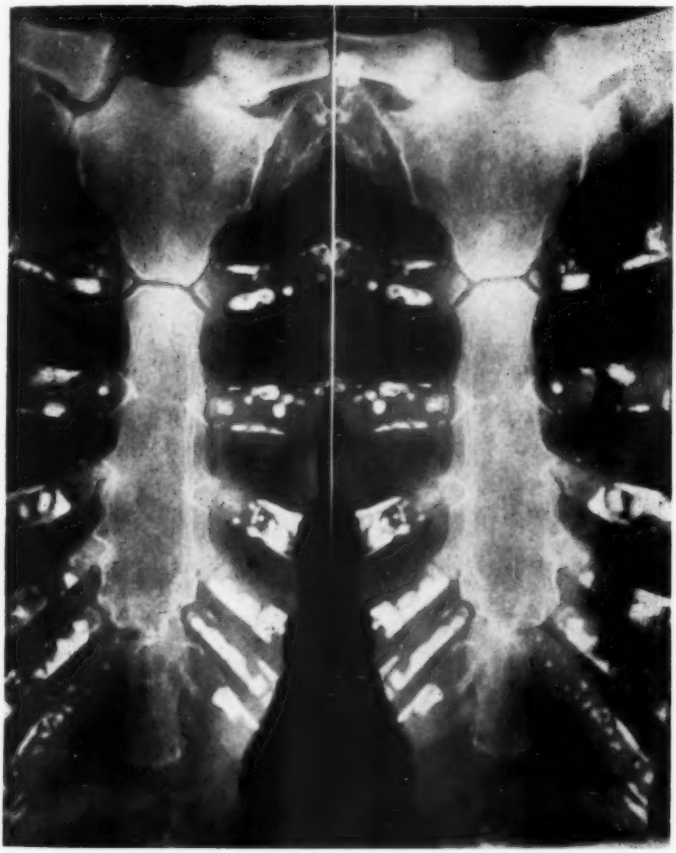

Fig. 3. Autoradiograph from back and front of a post-mortem specimen of sternum. The ipsilateral internal mammary nodes have drained lymph containing Au 198 from a previous intramammary injection. The film from the front of the sternum shows no exposure from the active glands owing to failure of the β-rays to penetrate the soft tissue of the intercostal space.

if unused there is still a single dose in a suitable volume nearly three weeks later. One disadvantage of expiring colloidal Au 198 is that it is used undiluted and its red colour may cause skin staining if it is injected subcutaneously.

Autoradiography

The specimen is spread out, orientated and fixed for about twenty-four hours, if autoradiographs are taken before the specimen is sufficiently fixed to retain its shape the active areas may become reorientated within

Fig. 4. Autoradiograph of the axillary contents of both sides and ipsilateral interpectoral tissue from a similar case to Fig. 3 ; the pins mark the position of the clavicles. There is uptake in the ipsilateral axillary lymph nodes but none in the contralateral axilla. The beaded pattern of some of the afferent lymph vessels is clearly demonstrated by the Au 198 they contain.

the tissue and the films cannot subsequently be compared with the cleared specimen.

The specimen is mopped dry, pressed as flat as possible, placed in a polythene bag, sandwiched between two paper covered X-ray films and left undisturbed for three to twenty-four hours; before the films are removed a soft tissue exposure is superimposed to facilitate orientation of the active areas. It is important to have a film on both sides of the specimen because the penetration of the β-rays is poor and the pictures differ if the specimen is more than a few millimetres thick.

Pictures obtained by this method provide the best illustrations of the distribution of lymphatic drainage that are available and this can be assessed quantitatively with counters when there are alternative pathways.

It is sometimes useful to inject a mixture so that more than one method of examination may be carried out in a single case. Thus a total volume of 1.5 ml. might contain any or even all of the following:

Patent blue—to show lymphatics during operation.

Iron dextran—to show lymphatics in cleared specimen.

Dionsil—to show extent of injection on radiograph.

Radioactive gold Au 198—to provide autoradiograph of regional drainage.

Xylocaine—is added to make the injection site pain free.

ACKNOWLEDGMENTS

These techniques were developed in the Bland Sutton Institute with the assistance of the staff of the Barnato Joel laboratories, and later in the Institute of Clinical Research at the Middlesex Hospital. My grateful thanks are also due to the members of the Surgical Staff and Mr. Vaughan Hudson in particular.

REFERENCES

Aselius, G. (1627) *De lactibus sive lacteis venis quarto vasorum mesaraicorum genere novo invento.* Milan.
Bloom, H. J. G. and Gregory (1958) Middlesex Hospital. Personal communication.
Cruikshank, W. (1786) *Anatomy of the absorbing vessels of the human body.* London.
Gerota, D. (1896) *Anat. Anz.* **12,** 216-224.
Gray, J. H. (1938) *Brit. J. Surg.* **26,** 462-495.
Handley, R. S. and Thackray, A. C. (1954) *Brit. J. Med.* **1,** 61-63.
Hultborn, K. A. Larsan, K. G. and Ragnhult, I. (1955) *Acta radiol (Stockh.)* **43,** 52-64.
Kinmonth, J. B. (1954) *Ann. Roy. Coll. Surg. Engl.* **15,** 300-315.
Mascagni, P. (1787) *Vasorum lymphaticorum descriptio et iconographia.* Siena.
Nuck, A. (1697) *Adenographia curiosa.* Leyden.
Selbie, F. R. (1938) *Brit. J. Exp. Path.* **19,** 100-107.
Turner-Warwick, R. T. (1955) *Lancet* **2,** 1371.

IMPROVEMENTS IN CORROSION CASTING TECHNIQUES

by

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PART 1

Improved methods for making corrosion casts of ducts and blood vessels with synthetic resin.

INTRODUCTION

In *Anatomical Techniques* (1956) the writer described in detail the use of Marco resin for filling all types of anatomical cavities. Since the publication of this book further experience has led to a number of improvements in the methods employed, particularly in vascular injections, which yield better casts with less labour. The purpose of this article is to make these technical advances available to those who are interested in this work.

Space permits the description only of those details which have been changed. For the rest of the practical information essential for success in this work reference should be made to *Anatomical Techniques*.

Fixation of material

Weak formalin solution is preferable to spirit for fixing the tissues (except lungs) when a resin injection is planned. Unlike spirit, formalin does not have to be washed out of the tissues before the resin is injected. Four per cent. formalin is suitable for general use, and 2 per cent. for fixing tissues which become excessively hardened in the stronger solution.

It is best to fix the organ only for a few days before the resin injection is made. Washing out of blood and fixation can usually be combined in a single operation. A fifteen litre aspirator is filled with formalin solution of the required strength, made up in deaerated water. This is allowed to flow by gravity into the vessels of the organ, which rests immersed in cold water. In those cases, as for example a limb, where the tissues are liable to become waterlogged before the blood has been removed from the veins, 2 per cent. sodium chloride is added to the formalin solution.

Occasionally it is advantageous deliberately to make the tissues turgid with fluid. In the case of the heart, which is fixed in 4 per cent. formalin injected via the aorta into the coronary arteries, the initial injection is made with an enema syringe. As much pressure is exerted as can be applied without risk of rupturing the aortic valves. The fixative is forced into the coronary arteries faster than it can escape via the cardiac veins. As the tissues of the heart become turgid, the heart assumes a moderately expanded form and is fixed in this position by the formalin.

Before the resin injection is commenced, there must be ample room in the tissues for the water displaced from the vessels and ducts. If the tissues are waterlogged, it is impossible to fill the vessels completely with

resin. This can be demonstrated in an organ like the heart, in which the principal vessels are superficial, so that the flow of resin can be observed during the injection.

To avoid too much water in the tissues at the time of the resin injection, perfusion of the vessels should always be stopped at least twenty-four hours before the resin is run in, so that excess fluid has time to escape. Additional treatment is sometimes necessary to remove fluid from the tissues. In the case of the heart the muscle is gently squeezed. Excess fluid can be siphoned from the arteries of a limb.

The kidney presents special difficulties if arteries, veins and pelvis are all to be filled, as the volume of water in these three cavities is great in proportion to the amount of glandular tissue into which water can be displaced. If the kidneys are injected with resin from the great vessels, escape holes must be provided for the water displaced from the vena cava and aorta respectively, so that the water in these vessels is not driven into the kidneys. The order in which the systems are filled is important. The veins, which are the most difficult to fill completely, are injected first, so that water displaced from them can escape both via the arteries and pelvis. The arteries are filled next. As their volume is small, little fluid is displaced from them. Before the pelvis is filled a needle prick is made through the uppermost part of its wall to allow water, displaced by the resin, to escape. Although resin may also escape from this hole, the rate of escape is so slow that it may be disregarded.

The problem of displacing water from cavities to be filled with resin has been stressed because in certain cases it is important. Some organs, however, such as lungs and liver, are so freely permeable to water when they have been fixed, that no problem of this kind is encountered.

The resin injection

To obtain a really good cast it is essential to inject the resin mixture as late as possible before it solidifies. If it is injected too soon, water in the tissues contaminates the surface layer and prevents it from setting properly. This results in a fragile cast of poor colour. Also, resin may impregnate the walls of vessels so that it is difficult to remove them from the cast. Sometimes the resin may even soak into the tissues and prevent satisfactory maceration by the acid.

It follows that the timing of the resin injection is the most important single factor in producing first-class casts. In *Anatomical Techniques* the writer recommended that the injection be timed by polymerising a test sample of the resin to establish the working life (i.e., the exact time the resin takes to solidify after the accelerator has been incorporated). Unfortunately, even small fluctuations in room temperature such as occur in most laboratories have a big effect on the working life, so that this method of timing is not really satisfactory.

This problem has been solved by using a resin mixture containing considerably more catalyst and accelerator than was normally added.

This mixture, formerly recommended only for filling delicate vessels such as the bronchial and coronary arteries, is made up as follows:

Marco resin 26 C	100gm.
Monomer C	30gm.
Catalyst H C H	6gm.
Accelerator E	6ml.

This is referred to as the *Standard* resin mixture as it is used for the great majority of anatomical injections. It can be represented briefly as (100 30 6 6). Variations in the composition of the resin mixture can also be expressed by numbers alone.

The important feature of this mixture is that there is a striking rise in its temperature several minutes *before* it sets. This increase of temperature indicates accurately the moment at which the injection should be commenced and so dispenses with the necessity for making a working-life test. If any change occurs in the room temperature after the accelerator has been added, this is automatically compensated for by the change in the rate at which the resin heats up.

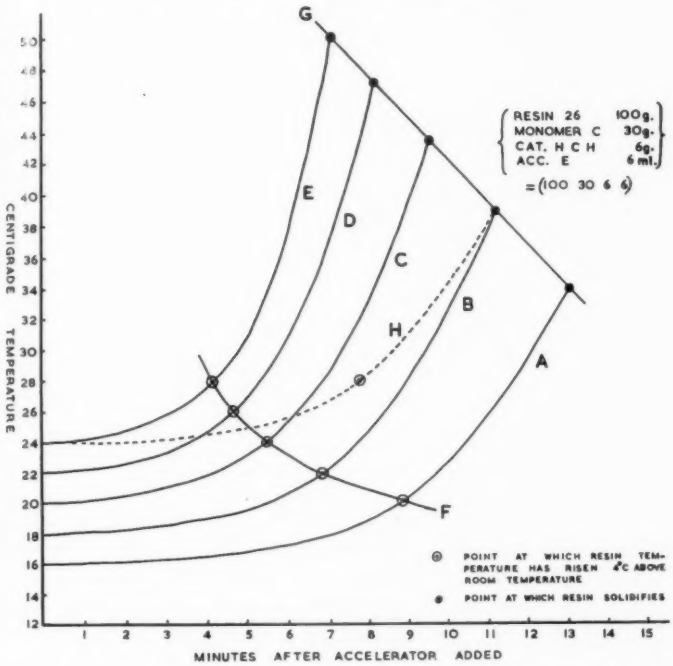
More accurate timing of the injection so greatly reduces the tendency for the resin to soak into the tissues that the relatively fluid mixture (100 30 6 6) can be used for all vascular injections. However, for filling the adult human bronchial tree the more viscous mixture (100 *15* 6 6) must be used.

Within the normal range of laboratory temperatures at which this type of work is done, viz., 16deg.C. to 24deg.C., the working life of the Standard mixture varies between seven and thirteen minutes. The behaviour of this mixture within this temperature range is illustrated by the graphs in Figure 1.

The injection is timed in the following way. The temperature of the resin mixture is adjusted so that it is exactly the same as the room temperature before the accelerator is added. After the accelerator has been incorporated, the resin is left standing in the beaker in which it is prepared until its temperature has risen four degrees centigrade. Then the injection apparatus is filled and the injection carried out. This timing allows between three and four minutes for the work to be completed (Fig. 1). This time is ample for the great majority of injections but, if a little more time is desired, the injection can be commenced when the temperature of the resin has risen three degrees centigrade instead of four.

A simple but efficient injection apparatus is required for this work. It must be capable of injecting a considerable volume of resin with whatever injection pressure may be necessary to ensure that the injection is completed before the resin solidifies. The Standard injection apparatus shown in Figure 2 is used. Injection pressure is applied as necessary by pumping air into the glass tube with an enema syringe.

Originally it was recommended that all systems be injected with resin simultaneously; but it is usually more satisfactory to inject them one



Curves A—E show behaviour of resin mixture (100 30 6 6) when polymerised at room temperatures between 16deg.—24deg.C. Curve F shows time taken by resin mixture (100 30 6 6) to heat up 4deg.C. at various room temperatures. Curve G shows relationship between working life of resin and temperature at which it solidifies. Curve H shows behaviour of mixture (100 30 4 4) at room temperature of 24deg.C. As less heat is generated by this mixture before it solidifies it is sometimes more suitable than (100 30 6 6) at this room temperature.

Fig. 1. Graphs illustrating the behaviour of the Standard resin mixture (100 30 6 6) at temperatures between 16deg.C. and 24deg.C., and the mixture (100 30 4 4) at 24deg.C. These graphs give all essential information to ensure perfect timing of injections within this temperature range.

by one. In certain cases the order in which the systems are injected is important. The reasons for this have already been explained in the case of the kidney. The problem is slightly different in the case of the lung, where the bronchial tree must always be injected last if the vessels are also being filled with resin. Otherwise the alveoli expand so much when partly filled with resin that they compress the walls of the blood vessels so that the latter cannot be completely filled.

Pigment pastes, previously recommended as alternatives to powdered pigments for colouring resin, should not be used for corrosion casting,

as the resistance of pigment pastes to the acid used to destroy the tissues is not generally as good as that of pigment powders.

Pruning of casts

Casts made by the improved methods are so much stronger that they can usually be pruned dry. In this condition the resin is brittle and so small branches can be broken off with a pair of dissecting forceps. Very small twigs are broken off with a probe. Spectacles should always be worn while this work is being done to protect the eyes from flying fragments.

This method of pruning is much quicker than the former one. in which the cast was kept flexible by frequent immersion in hot water and the twigs cut off with scissors. However, immersion in hot water is still necessary in certain cases. This is illustrated by the following example. A cast was made of the pulmonary arteries, pulmonary veins and bronchial tree of a very young child. The red resin used to fill the pulmonary arteries entered the pulmonary veins also, so that the cast of the latter was composed of a mixture of red and blue resin. This spoilt the specimen, but, by frequently immersing the cast in water at 50deg.C., so that it was kept flexible, it was possible to cut away the imperfect cast of the pulmonary veins piecemeal with bone forceps, without any damage to the cast of the arteries and bronchial tree. The kidneys provide another example of the use of hot water to make a cast flexible and so easier to handle without damage. A cast of the renal arteries can usually be separated from a cast of the pelvis and calices without damage to either, if the casts are kept flexible by immersion in hot water during the operation.

Repairs to casts

It is advisable to keep any branches broken accidentally from casts but not worth replacing. These sometimes form a useful basis for making repairs or for completing an imperfect cast. Once a slender branch has been cemented into the required position it is a simple matter to build up its thickness with resin cement suitably coloured. The resin cement formerly recommended (see *Anatomical Techniques*, p. 104) for this work should be thickened by adding some powdered Vinylite VYHH resin (obtainable from the Bakerlite Co. Ltd.), immediately after the accelerator has been incorporated. Sufficient is added to increase the viscosity of the mixture so that it can be applied where required without running.

Plasticine can often be used to hold a piece of resin in position until it is fixed with cement. When this method is not practicable, the piece is stuck to a length of thin copper wire with a quick-drying cement made by dissolving X-ray film in acetone. It is a comparatively simple matter to fix the wire so that the resin branch is held in exactly the required position while it is cemented in its correct place. Afterwards the copper wire is

detached by dissolving the celluloid cement with acetone applied with a small paint brush.

Availability of Marco resin

Workers in various parts of the world have found difficulty in obtaining resin suitable for this work. Marco resin 26 C is exported under the trade name of Markon 7 H.V., and Marco resin 28 C as Markon 9 H.V. Scott Bader & Co. Ltd. have undertaken to send small quantities of these resins and other components required for medical work to any part of the world where they would not otherwise be available ; but as the materials have to be transported through hot countries under refrigeration, they should be obtained from the nearest place where they are manufactured.

For general work the following quantities of the various components are recommended :

Marco resin 26 C (*packed in quart tins*)	12lb.
Marco resin 28 C	2lb.
Monomer C (*packed in quart tins*)	6lb.
Catalyst H C H powder	1lb.
Accelerator E	1lb.
Crystic powdered pigment red lake M.11	8oz.
Crystic powdered pigment blue M.21	8oz.
Crystic powdered pigment brilliant yellow M.17	8oz.

These quantities form a package reasonably easy to handle. The resin, monomer and accelerator must be stored in a refrigerator. If received in satisfactory condition they will keep for two years or longer.

PART II

Improved methods for making corrosion casts from the heart in synthetic resin

INTRODUCTION

The writer described a method of making corrosion casts of the cavities and blood vessels of the heart in *Thorax* (1954). The details of this technique were included in *Anatomical Techniques*, which also gave a method of making a cast of the coronary arteries alone.

The methods employed have been radically altered and a striking improvement achieved in the quality of the casts. The principal steps in the new methods are given below.

Fixation of the heart

Before a satisfactory corrosion cast of the cavities and blood vessels of the heart can be made, the organ must be fixed without gross distortion or excessive hardening. The cavities and blood vessels must be completely freed from blood.

The heart is placed in a bowl of cold water in the sink. It is manipulated to displace all air from its cavities and from the coronary arteries. A cannula, connected to the cold-water tap by rubber tubing, is inserted via

the cut ends of vessels into each ventricle in turn and any blood clots washed out by directing a strong jet of water into it.

A flanged glass cannula of appropriate size is tied with string into the cut end of the ascending aorta. Four per cent. formalin made up in deaerated water is injected into the cannula by means of an enema syringe with sufficient force to make the tissues turgid, but the injection pressure must not be so great as to rupture the aortic valves, which play an important role in the subsequent resin injection. When the tissues of the heart become turgid, the cavities expand moderately. The cannula in the aorta is then connected to a fifteen-litre aspirator filled with 4 per cent. formalin made up in deaerated water. The fixative flows by gravity into the aorta, through the coronary arteries and escapes via the cardiac veins, the aortic valves being held in the closed position by the pressure of the fixative. Perfusion is continued for four days, the aspirator being recharged when necessary. This treatment removes all traces of blood from the vessels and fixes the heart with the cavities expanded.

It is best to make the resin injection soon after fixation has been completed, but successful casts can usually be made several weeks later if the heart is stored in 4 per cent. formalin.

The perfusion of the heart with fixative must be stopped at least twenty-four hours before the resin is injected, to allow sufficient time for the surplus fluid to diffuse out of the tissues. Shortly before the resin is injected the heart tissues are gently squeezed to remove more of the fluid, as the success of the injection depends on there being ample room in the tissues for fluid displaced by the resin from the vessels.

Cast of the coronary arteries alone

The coronary arteries are injected via the aorta. The aortic valves, fixed in the closed position, prevent the resin flowing into the left ventricle. The Standard apparatus is used, 200ml. of the Standard resin mixture being prepared. Figure 2 shows the apparatus immediately before the injection is commenced. During the injection the heart rests in water at 30deg.C. For the first thirty seconds moderate injection pressure is applied by means of the enema syringe. When the resin appears in the small superficial arteries, the glass tube is topped up with resin and the injection apparatus left undisturbed until the resin sets, any further flow of resin being due to gravity. The application of injection pressure by means of the enema syringe immediately before the resin solidifies invariably causes the rupture of the aortic valves, which lose some of their strength as a result of contact with the resin.

Full details of the subsequent work, which comprises the destruction of the original tissues in concentrated hydrochloric acid, washing away of the macerated tissue from the cast, pruning of the cast, spraying it with Marco resin 28 C and mounting in a Perspex box, are given in *Anatomical Techniques*.

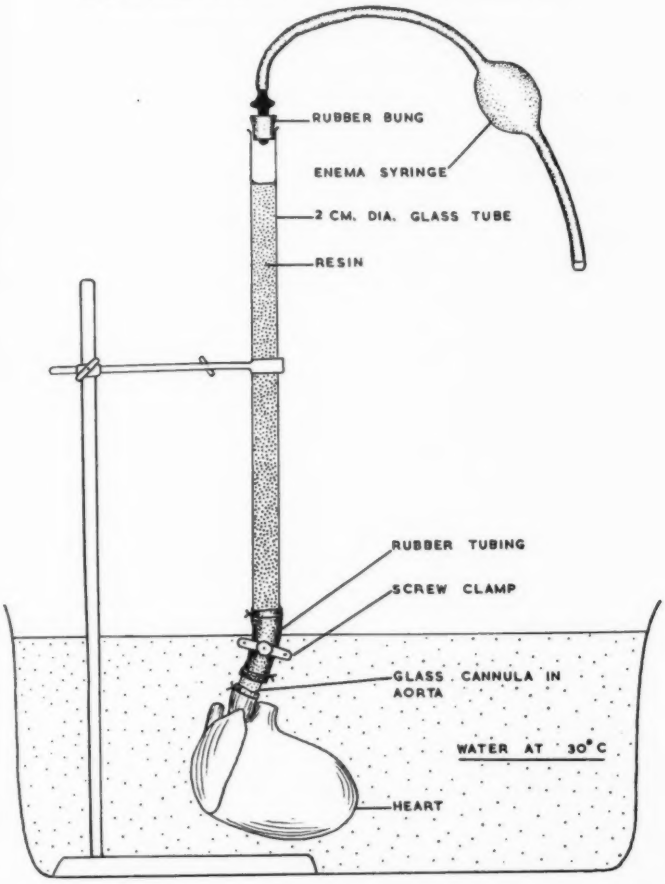


Fig. 2. Standard injection apparatus, so named because it is used for the great majority of resin injections. It is easily constructed in the laboratory. The gravitational flow of the resin can be strongly assisted by air pressure applied with an enema syringe. Resin which sets in the glass tube can be removed with a ramrod, after the tube has been boiled for half an hour in water containing a little detergent.

Cast of the left atrium and ventricles together with the coronary arteries

400ml. of the Standard resin mixture are required. Standard apparatus is connected to one of the pulmonary veins and to the ascending aorta. A cannula is tied to another pulmonary vein to serve as an escape hole for water displaced from the atrium by resin. The cut ends of the other two pulmonary veins are ligated.

To prevent the comparatively large bulk of resin which is required to fill the atrium and ventricle from overheating and cracking after it has solidified, the heart must be cooled by immersion in water at about 10deg.C. during the resin injection. The glass tube connected to one of the pulmonary veins is filled with resin. This is allowed to flow into the atrium and ventricle. Water displaced from the atrium escapes via the escape cannula, which is closed as soon as resin free from water flows from it. Water in the ventricle is displaced into the glass tube attached to the ascending aorta. The flow of resin may be accelerated by pressure exerted with the enema syringe. During the filling of the cavities of the heart it is essential that the apex of the ventricles points downwards, as otherwise water is trapped within. Apart from causing an incomplete cast of the left ventricle, water trapped within it may be displaced into one of the coronary arteries after these have been filled with resin but before the resin has solidified. If this happens an imperfect cast of the coronary artery is also produced.

As soon as the cavities of the left side of the heart are full of resin, more resin from the tube connected to the pulmonary vein is driven, by means of air pressure from the enema syringe, through the cavities into the glass tube connected to the aorta, until the tube is full of resin. Water already in the tube is allowed to overflow from its upper end. At this stage the level of resin in the tube attached to the pulmonary vein should be low to avoid too much distension of the atrium. Firm injection pressure is now applied by means of the enema syringe to the resin in the glass tube attached to the aorta. The aortic valves prevent backflow of resin into the ventricle while the coronary arteries are being filled. When the coronary arteries are full of resin, the apparatus is left undisturbed until the resin has set.

The important feature of this method is that, provided the aortic valves have been fixed in the closed position, the ventricles are filled with resin at low injection pressure, while a relatively high injection pressure of the coronary arteries is achieved.

Water is lighter than the resin and so floats on top of it. Sometimes in this and similar injections one or more pockets of water are trapped above the resin, as for example in the tied end of a pulmonary vein. The water is removed before the resin has solidified by pricking the wall with a stout needle. This allows the water to escape and be replaced by resin, but the escape of resin from needle pricks is negligible.

After the resin has solidified, it is advisable to examine the heart carefully. If in spite of all precautions there is a pocket of water in a cavity, or an artery incompletely filled because of an air lock, these defects can be remedied by injecting resin from a hypodermic syringe. An all-glass syringe should be used and, in the case of a vessel, a needle smaller than the vessel, as this allows resin to flow in both directions from the point at which the needle is inserted. When a vessel is being filled in this way, the risk of transfixing the vessel wall is reduced if the needle is bent

somewhat. The injection must be stopped before the resin solidifies so that the syringe can be flushed out with acetone. If the resin sets in the syringe it is usually impossible to separate the piston from the barrel. The needle can be left in position in the vessel until the resin is almost solid. Most of the resin in it can then be expelled with a piece of wire, and the needle thoroughly cleaned by flushing out the remains of the resin with acetone.

Cast of the right atrium and ventricle with the cardiac veins

A heart must be selected in which the foramen ovale is closed. This can be established by injecting water into the right side via the superior

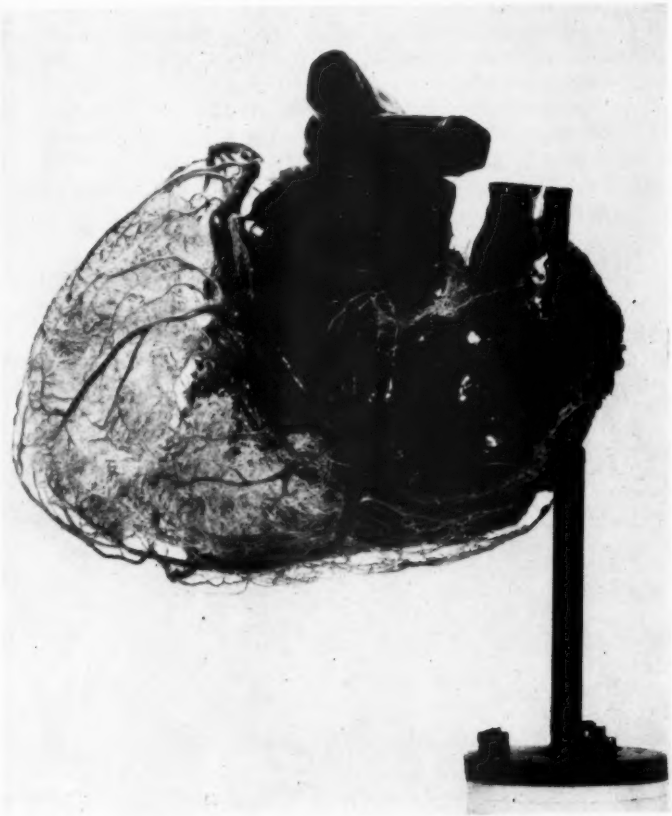


Fig. 3. Posterior view of a cast of the right atrium and ventricle, with cardiac veins. × 2/3.

vena cava after the cut ends of the inferior vena cava and the two pulmonary arteries have been closed. A patent foramen ovale is very common and allows a free flow of resin from the right atrium into the left. A valve-like flap prevents flow in the reverse direction so that the cavities of the left side can be filled with resin satisfactorily.

The heart is injected with resin while immersed in water at about 10deg.C. 400ml. of Standard resin mixture are prepared. The resin is injected via the superior vena cava. The water in the right atrium is allowed to escape through a cannula tied into the inferior vena cava. The water displaced from the right ventricle escapes through a cannula tied into one of the pulmonary arteries. The other pulmonary artery is ligated. It is essential that when the injection of the resin is commenced the escape cannulae are open ; otherwise water is driven into the cardiac veins which cannot subsequently be filled completely with resin. During the initial injection the apex of the ventricle must point downwards to prevent water being trapped in it.

When the cavities have been filled with resin the glass injection tube is filled to the top with resin. This is forced down into the cavities of the heart by pressure exerted with the enema syringe. The right atrium and

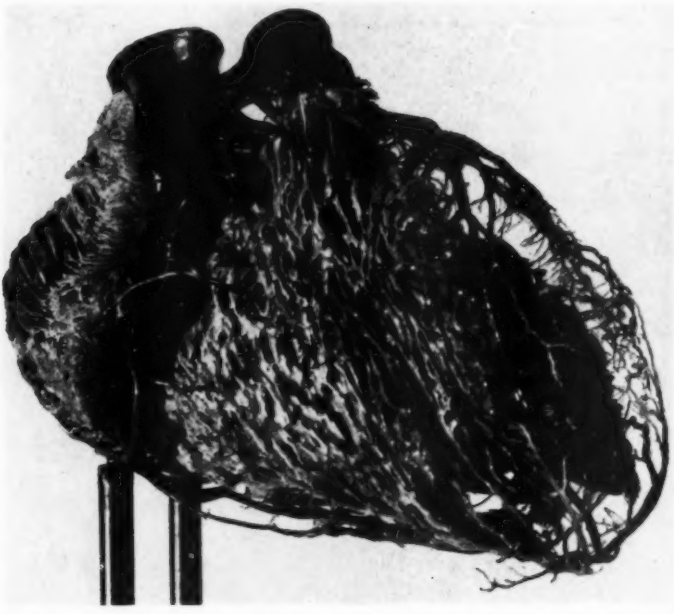


Fig. 4. Anterior view of a cast of the cavities and blood vessels of the heart. × 2/3.

ventricle expand greatly under comparatively slight pressure, so care is needed to avoid driving all the resin and air as well into the atrium. The pressure is maintained for a few seconds and then released by detaching the enema syringe from the glass tube. This treatment is repeated several times to ensure complete filling of the cardiac veins. Then resin is allowed to escape from the cannula attached to one of the pulmonary arteries until the level of resin in the tube attached to the superior vena cava is only just above the level of the water in which the heart rests. This prevents unnatural distension of the cavities. The apparatus is left undisturbed until the resin sets. Figure 3 shows a cast made by this technique.

Cavities and vessels of both sides of the heart

The procedure is the same as that used to fill the cavities and vessels of one side of the heart. The left side is filled first, the other side being filled about an hour later, when the resin first injected has become fairly hard. The day after the injection is completed the two casts are cemented together with clear resin after adjacent areas of the walls of the two atria, and of the aorta and pulmonary trunk respectively, have been dissected away. While this work is being done care is needed to avoid damage to the cast of the vessels. It is best to do it with the heart resting on cotton wool and partly immersed in water. Figure 4 shows a cast prepared by this method.

Cast of the coronary arteries and cardiac veins alone

The cavities and vessels of both sides of the heart are filled with resin by the method described above. The next day, the heart is dissected to expose the resin casts of the two coronary arteries where they arise from the aorta. The casts of the anterior cardiac veins are exposed where they enter the right atrium, also the cast of the coronary sinus where it enters the atrium. The resin cast is cut through by means of dental burrs at the points where it has been exposed. The arterial and venous casts are cemented together with clear resin at several points where the artery and vein run close together, after the walls of the adjacent vessels have been removed.

After maceration the cast is thoroughly washed and then placed in water at about 45deg.C. This makes the cast of the vessels sufficiently flexible to enable the cast of the cavities to be removed without breaking the cast of the vessels. It may be necessary to cut through the cast of one or two vessels to facilitate the removal of the cast of the cavities ; but in this case the cast of the vessels can easily be cemented together again with resin cement.

The cast of the vessels is dried and strengthened by drops of clear resin cement which fix the cast of the arteries and of the veins together. The cast of the coronary arteries can be reinforced by cementing a slender rod of clear resin across the gap between their cut ends. The somewhat fragile cast is greatly strengthened by the final spraying with Marco

resin 28 C, as this fixes many of the very small branches, which are almost touching, together. Figure 5 shows a photograph of a cast prepared by this method. The casts of the cavities of the two sides of the heart can also be mounted separately.

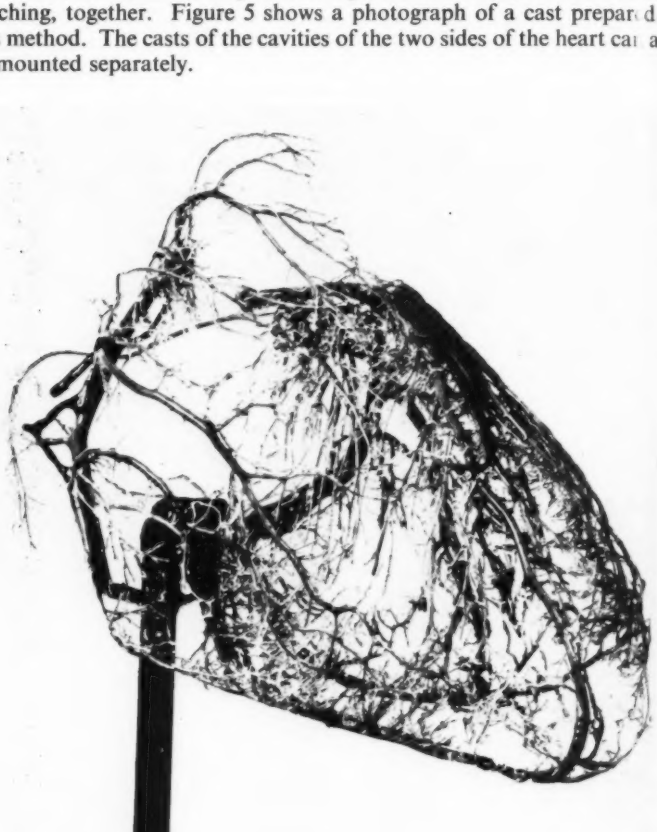


Fig. 5. Cast of coronary arteries and cardiac veins alone. × 2/3.

Cavities and blood vessels of the heart, with bronchial tree and vessels of the lung

This is an arduous undertaking, the most tedious part of which consists of the pruning of the cast. Special care is required during pruning to preserve the delicate cast of the bronchial arteries. But provided that the material used for this technique reaches the laboratory in perfect condition, an almost perfect cast can be obtained.

Before washing out of the blood is commenced, any air trapped in the right ventricle is drawn off by means of a hypodermic syringe, the needle

being passed through the ventricular wall. After the blood has been washed out with deaerated water, the lungs are deaerated by the method described in *Anatomical Techniques*. The material is fixed in 4 per cent. formalin for two days before being prepared for the resin injection. Fixation should not be more prolonged, as formalin destroys the elasticity of the lungs if they are left in it for longer than this.

Before the resin injection is commenced, the formalin must be washed out thoroughly. If any appreciable amount of formalin remains in the lungs, it causes the gelatine, with which the lungs are filled before the injection of the bronchial tree with resin, to solidify.

After they have been washed out, the lungs and heart are placed in water at 10deg.C. The lungs are expanded by filling them via the trachea with cold deaerated water.

The cavities and blood vessels of the left side are filled first, by means of a cannula tied into the appendage of the left atrium. 600ml. of the Standard resin mixture are required. The lungs and heart are placed on a Perspex tray shaped roughly like the posterior wall of the thoracic cage (see *Anatomical Techniques*, Fig. 32). During the initial injection, the tray and specimen must be tilted so that the apex of the ventricle points downwards, to prevent water being trapped in the ventricle.

After about an hour the right side is filled with resin, 600ml. being required. Finally, after a further hour, the lungs are filled with gelatine solution via the trachea and the bronchial tree is filled with resin by the method described in *Anatomical Techniques*, except that the mixture (100 15 6 6) is used and the injection timed by the new method described above. It is advisable to cement the three casts, viz. : the left side of the heart with vessels, the right side of the heart with vessels, and the bronchial tree, together before maceration of the tissues.

REFERENCES

TOMPSETT, D. H. (1954) *Thorax* **9**, 123.
————————(1956) *Anatomical Techniques*. Edinburgh and London, Livingstone.

ANATOMICAL MUSEUM

THE SPECIAL DISPLAYS have now been resumed and that for February shows some interesting Hunterian examples of growth and reproduction.

RECENT OVERSEAS VISITORS TO THE COLLEGE

RECENT OVERSEAS VISITORS to the College have included Professor B. N. Sinha, orthopaedic surgeon at Lucknow, who attended the monthly dinner in January.

JOHN HUNTER'S GIRAFFE

by

Jessie Dobson, B.A., M.Sc.

Curator of the Anatomy Museum, Royal College of Surgeons of England

IN 1780, THE skin of a fine male giraffe was brought to England and presented to John Hunter who had it stuffed and mounted for exhibition in his most remarkable museum (Fig. 1). This was yet another testimony

to the unique character of this collection for it was the first specimen of a giraffe ever to be seen in England and naturally it excited the greatest interest then as, indeed, the recollection of this fact should do now.

The giraffe is native to the African continent but that it was formerly more widely distributed is known from fossil remains found in Pliocene

deposits in Greece, Persia, India and China. Perhaps the earliest pictorial record of the animal is that found on the monuments of Thebes where chiefs of four different nations were shown bringing tribute and gifts to Tuthmosis III during whose reign it is supposed that the Israelites quitted Egypt. Writing in the year 260 B.C., the Sicilian Timaeus mentions that among the animals found near the equator "the giraffe is the most wonderful, both for the beauty of its form, and the extraordinary manner of its production. For they say that the giraffe proceeds from a female Ethiopian camel, a wild cow and a male hyaena: for in Ethiopia, the male hyaena pairing with a female camel, she gives birth to a young one partaking of the natures of both parents: and if this happens to be a male, and to pair in its turn with a wild cow (the addax antelope) the result of this second cross is the giraffe."

Strabo (64 B.C. to A.D. 21) mentions the "camelopardalis," an animal, he says, "not at all resembling a panther, as might be imagined; for in the variegation of its colours it more resembles a fawn, and is marked with striped hairs; the hind quarters are lower than the fore, seeming to settle down towards the tail, where it is not higher than an ox, whereas the fore-legs are as high as those of a camel: the neck is straight and raised to a great height, so that to the top of the head it is much taller than a camel. From this disproportion of parts, I should not think the animal likely to possess the extraordinary swiftness attributed to it by Artemidorus, who says that nothing can overtake it."

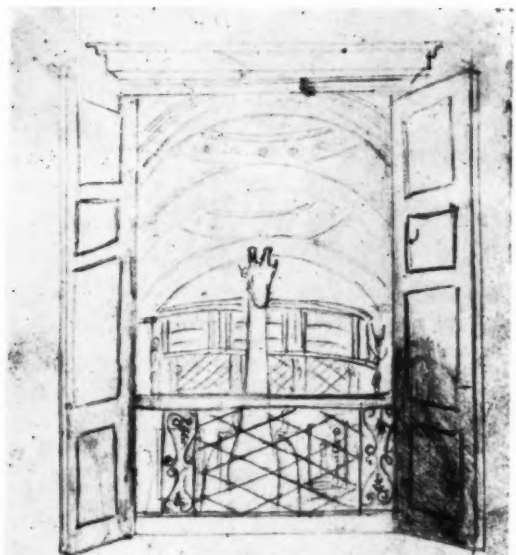
Pliny gives the information that Julius Caesar was the first to bring the giraffe to Rome, an innovation that appears to have been popular for Pausanius, writing in the second century A.D., mentions that he had seen at the Roman games "Indian camels spotted like panthers."

No mention is made of the horns until the time of Oppian, who died in A.D. 213 at the age of thirty. His description is remarkably accurate, particularly in his observation that the so-called horns do not consist of horny substance, and in his allusion to the tufts of hair with which they are tipped. That he had seen a live giraffe is obvious from his mention of the brilliancy of the eyes and of the halting motion of the hind limbs. It was possibly the Gordian family who imported them for their magnificent entertainments where it was not unusual for hundreds of deer, wild horses and ostriches to be shown; and it is known that the third emperor of this name kept in his private menagerie a hippopotamus, twenty onagers and ten giraffes.

After the inauguration of Constantinople as the capital of the Eastern Roman Empire, the giraffe was less frequently seen in Europe and it became almost legendary. Indeed, Heliodorus, at the end of the fourth century, mentions a gift brought to the emperor of "an animal of strange and wonderful form, in bulk almost equal to a camel . . . its eyes appeared as if painted, and it rolled them strangely. . . . Its appearance struck the whole multitude with astonishment."

The rarity-value of the animal continued to make it eminently suitable as a choice gift for several hundred years. In 1260, the emperor Michael Palaeologus received one from the sultan of Egypt—the last to be seen in Constantinople previous to the Turkish conquest in 1453. In the fifteenth century, two specimens were sent to Europe, one to Frederick III, the other to Lorenzo di Medici, after which time none was seen in this continent until the end of the eighteenth century. The distinguished Swedish naturalist, Fridericus Hasselquist, a pupil of Linnaeus, in the account of his voyages in the Levant in 1752, refers to the giraffe as a "camel deer" and was able to describe it only from a skin that he saw at Suez.

It is indeed curious that Oppian, writing in the third century, was better able to give an accurate description of the animal than were the naturalists of the eighteenth century and it is no wonder, therefore, that John Hunter's specimen should have attracted such attention. As is well known, he spared no pains to secure the rare or unusual for his museum



a View of the Museum from the Cabinet Room. 1812

and it was probably at a meeting at the Royal Society that the idea of obtaining a specimen of a giraffe first presented itself. On 25th January 1770 a letter was read to the assembled Fellows from Captain Carteret of H.M.S. Swallow giving the information that a party sent out by the Governor of the Cape of Good Hope had found two giraffes, one of which they captured. Unfortunately, it died in captivity but the skin was preserved and sent to the Natural History Museum at Leyden. Captain Carteret gave the dimensions and sent a drawing of the animal, stating that, as the existence of this scarce and curious creature had been doubted by many, the Society could make any use of the information that they desired.

Ten years were to elapse, however, before John Hunter received his specimen. This, the skin of a fine male, was brought to this country by Lieutenant Paterson by whom it had been shot in the interior of Caffraria and it was presented to Hunter by Lady Strathmore who had financed Paterson's expedition. The skin, still containing the skull, cervical vertebrae and trachea and several other parts of the skeleton, was stuffed and mounted separately as were the individual bones (Owen's Catalogue Nos. 3618 and 3621-3639 Ost.). The trachea appeared as three specimens in the *Physiological Series* (Owen's Catalogue Nos. 1150-1152). In fact, not one portion was wasted for, from the disposition of the elastic ligaments of the neck, Hunter was able to draw conclusions as to their effect in assisting the muscles to maintain equilibrium.

John Hunter died in 1793, his collection was bought by the government and placed in the custody of the Company of Surgeons in 1799, and our giraffe took a prominent position in the museum erected to the design of George Dance early in the following century (Fig. 2). Thirty years later, however, it was found that this building was no longer adequate for the proper display of the greatly increased number of specimens. The whole collection was placed in store while Dance's building was demolished and an entirely new series of museum and other rooms were built according to the plan of Sir Charles Barry. It was then that it was decided that the series of stuffed animals, most of them Hunterian, was extremely difficult to accommodate. With considerable difficulty, permission was gained in May 1834 from the Lords Commissioners of the Treasury and ratified by King William IV to transfer these specimens, thirty-one in all, to the British Museum. As well as the giraffe there were a tapir, a llama, a giant kangaroo and a black swan and it is difficult to understand now why these specimens, so rare in collections of that period, should have been allowed to leave the College.

But this was not the end of the story. In the following year, a Select Committee was set up to enquire into the affairs of the British Museum. Comments were made on the high standard of exhibits of stuffed animals in the Jardin des Plantes in Paris and on the poor display of such preparations in the British Museum. In evidence, James de Carle Sowerby

stated that the poor condition arose " from want of taste in the persons employed to stuff the animals in various instances . . . the giraffe upon the staircase is very stiff " ; and R. E. Grant remarked on " some stuffed skins that once resembled the giraffe." Similarly, E. T. Bennett maintained that " it was probably never good and is certainly now very miserable." John G. Children, also giving evidence, said " Mr. Paterson's giraffe has been exposed for years in the same way in the Museum of the College and is certainly not likely to be further influenced in the slightest degree by its present exposure ; it is exposed because there is no possibility of covering it "— which was reasonable enough.

When the giraffe was finally disposed of is not known but obviously the long exposure to the deleterious influences of dust and atmospheric conditions generally were in the end the cause of its ultimate disintegration. After all, a museum life of over fifty years for a natural skin that even in its heydey was probably but imperfectly preserved and stuffed is remarkable enough, and though we may regret the loss of one of the most interesting of John Hunter's specimens, we can still be proud of the fact that our museum once housed the first preparation of a giraffe to be seen in this country.

HONOURS CONFERRED ON FELLOWS AND MEMBERS

IN THE NEW Year Honours List H.M. The Queen graciously conferred the following honours on Fellows and Members of the College :

C.B.E. (Military Division)	C. B. Nicholson, M.R.C.S.
C.B.E. (Civil Division)	A. R. Culley, M.R.C.S.
	J. A. James, F.R.C.S.
	E. E. Pochin, M.R.C.S.
	K. Robson, M.R.C.S.
M.B.E. (Civil Division)	Miss J. C. Clatworthy, M.R.C.S.
	C. G. Seymour, M.R.C.S.

The Ophthalmological Societies of New Zealand, Australia and South Africa have elected Mr. B. W. Rycroft, O.B.E., M.D., F.R.C.S., to the Honorary Membership of their Societies.

DONATIONS

THE FOLLOWING GENEROUS donations have been received during the last few weeks :

£5,000	Mr. W. R. Gibson, F.R.C.S. (further gift).
$300	Mrs. R. J. B. Denby (*per* Mr. Simon Vos).
£105	Mr. R. H. Paramore, F.R.C.S.
£100	Mr. H. J. Windsor, F.R.C.S.

Sir Victor Negus and Mr. J. M. Craig, F.R.C.S., have undertaken to make annual donations to the Restoration and Development Fund for seven years under covenant, and Professor G. W. Causey, F.R.C.S., has undertaken a voluntary annual subscription to the College for seven years under covenant.

BOOKS ADDED TO THE LIBRARY, OCTOBER-DECEMBER 1958

Anaesthesia

EVANS. Modern trends in anaesthesia. 1958. Editor's gift.
FINSTERER. Local anaesthesia, methods and results in abdominal surgery. 1923. Gift of Sir Russell Brock.

Anatomy

ADAMS. Carotid body and carotid sinus. 1958.
APPLETON AND OTHERS. Surface and radiological anatomy. 4th edition. 1958.
CUNNINGHAM. Manual of practical anatomy. 12th edition, vol. 2. 1958.
GRANT. A method of anatomy. 6th edition. 1958.
TANDLER. Topographische Anatomie dringlicher Operationen. 2nd edition. 1923. Gift of Sir Russell Brock.

Biochemistry

PFIZER CO. The Pasteur fermentation centennial : a scientific symposium. 1958. Publisher's gift.
SYLVEN AND MALMGREN. Histological distribution of proteinase in solid tumour transplants. 1958.

Cancer

BIGNALL. Carcinoma of the Lung. 1958.
PACK AND ARIEL. Tumours of soft somatic tissues. 1958. Author's gift.
RAVEN. Cancer of the pharynx, larynx and oesophagus and its surgery. 1958. Author's gift.
RAVEN (Editor). Cancer, vol. 4. 1958. Editor's gift, continuation.

Dental Surgery

BRAUER. Dentistry for children. 4th edition. 1958.
MOORREES. The Aleut dentition. 1958.
RUSHTON AND COOK. Oral histopathology. 1958.
SALZMANN. Orthodontics. 2 vols. 1958.
SCOTT AND SYMONS. Dental anatomy. 2nd edition. 1958.
SHAFER. A textbook of oral pathology. 1958.
THOMA. Oral surgery. 3rd edition. 1958.

Endocrinology

LISSER AND ESCAMILLA. Atlas of clinical endocrinology. 1958.

Laryngology

FIORETTI. La tonsilla palatina. 1957. Author's gift through Sir Victor Negus.
NEGUS. Comparative anatomy and physiology of the nose and paranasal sinuses. 1958. Author's gift.

Medicine

BÜRGER. Geschlecht und Krankheit. 1958. Gift of Sir Henry Souttar.
DAVIDSON. Principles and practice of medicine. 4th edition. 1958.
DUNLOP. Textbook of medical treatment. 7th edition. 1958.

Neurology (see also Surgery, neurological)

BOWDEN. Peripheral nerve injuries. 1958. Gift of Professor Lambert Rogers.
DOW AND MORUZZI. Physiology and pathology of the cerebellum. 1958.
WALSHE. Diseases of the nervous system. 9th edition. 1958.

Ophthalmology

DUKE-ELDER. System of ophthalmology. Vol. 1. 1958.

Orthopaedics

ADAMS. Outline of fractures. 2nd edition. 1958. Gift of Professor Lambert Rogers.
GERVIS. Orthopaedics in general practice. 1958. Gift of Messrs. William Heinemann.
HACKETT. Ligament and tendon relaxation. 3rd edition. 1958. Gift of Mr. St.J. D. Buxton.
KLAPP. Das Klapp'sche Kriechverfahren. 3rd edition. 1958. Gift of Sir Henry Souttar.
PERKINS. Fractures and dislocations. 1958.
TIETZ UND KLAUS. Rechtlinien für die sportärzliche Untersuchungen. 1958. Gift of Sir Henry Souttar.
WYNN PARRY. Rehabilitation of the hand. 1958.

Paediatrics

GAIRDNER. Recent advances in paediatrics. 2nd edition. 1958.

BOOKS ADDED TO THE LIBRARY

Pathology

ANDERSON. Pathology. 3rd edition. 1957.
MUIR. Pathology. 7th edition. 1958.
NETTER. Liver, biliary tract, and pancreas (Ciba Medical Illustrations, vol. 3). 1958, Gift of Ciba Co.
RIDDELL AND STEWART. Fungous diseases. 1958.
WRIGHT. Introduction to pathology. 3rd edition. 1958. Gift of Messrs. Longmans.

Pharmacology

PFIZER CO. Report of a symposium on clinical trials at the Royal Society of Medicine. 1958. Publisher's gift.

Physics in Medicine

ROBERTS AND OTHERS. Electrolyte changes in surgery. 1958. Gift of Professor Lambert Rogers.
VEALL AND VETTER. Radioisotope techniques in clinical research and diagnosis. 1958.

Physiology

WEBER. Motility of muscle and cells. 1958.

Surgery

BAILEY. Emergency surgery. 7th edition. 1958.
GILLIS. Modern trends in surgical materials. 1958.
HARLOW. Atlas of surgery. 1958. Two copies, gifts of Sir Cecil Wakeley and Professor Lambert Rogers.
KIELY. Textbook of surgery. 2nd edition. 1958. Gift of Sir Cecil Wakeley.
MYBRUGH. Causes and treatment of abdominal adhesions. 1953. Gift of Sir Russell Brock.
OLIVER. Basic surgery. 1958.
WAKELEY. Synopsis of surgery. 15th edition. 1958. Editor's gift.

Surgery, neurological

MENTHA. Bases physiologiques de la chirurgie neurovasculaire. 1957. Gift of Professor Lambert Rogers.
PATERSON ROSS. Surgery of the sympathetic nervous system. 3rd edition. 1958. Gift of the author, the President.

Surgery, plastic

BROWN AND MCDOWELL. Skin grafting. 3rd edition. 1958.

Surgery, thoracic

BORRIE. Management of thoracic surgical emergencies. 1958.
FRANCIS AND CURWEN. Major surgery for pulmonary tuberculosis, part 1. 1958.

Urology

RICHES. Malignant disease of the urinary tract (Lettsomian lectures). 1958. Author's gift.

Reference Books

IZQUIERDO. Catalogue of the library of the department of physiology, Mexican National University. 1958. In Spanish. Gift of University College, London.
JABLONSKI. Russian-English medical dictionary (National Library of Medicine, Washington). 1958.
SCIENTIFIC AND LEARNED SOCIETIES OF GREAT BRITAIN. 1958.

HISTORICAL LIBRARY

Historical Texts

F. M. VAN HELMONT. Alphabeti naturalis Hebraici delineatio. (A method of teaching deaf-mutes). 1667.
ROBERT BOYLE. Medicinal experiments. Vol. 3. 1694. Both presented by Dr. S. D. Adam and Miss Adam.
ROYAL COLLEGE OF SURGEONS. Lecture notice (Broadsheet). 1816.
PATHOLOGY. Anonymous article (372 pages) from Encyclopaedia Londinensis. 1823. Gift of the Honorary Librarian, Sir Geoffrey Keynes.
JONES QUAIN. Anatomical plates. 4 vols. 1836-42. Gift of Dr. J. F. Hughes. Deposited in the Anatomical Department.
ROBERT WILLIS. On the signification and ends of the portal circulation. 1841. On the function of the lymphatic vessels. 1844.
Dr. Willis was the first librarian of the College (1828-45).

BOOKS ADDED TO THE LIBRARY

History of Medicine

CASTIGLIONI. A history of medicine, translated by E. B. Krumbhaar. 2nd edition. 1958.

GUTHRIE. History of medicine. 2nd edition. 1958.

RICHARDSON. The surgeon's tale, a story of modern surgery. 1958.

BURROWS. History of medicine in South Africa. 1958. Gift of Mr. H. Grant Whyte.

INGLIS. Hospital and community, a history of the Royal Melbourne Hospital 1958.

LASSEK. Human dissection, its drama and struggle. 1958.

FIORETTI. La scoperta degli ossicini auricolari. 1958. Author's gift, through Sir Victor Negus.

Biography

James Cook. PRICE. The explorations of Captain Cook in the Pacific from his own journals, 1768-1779. 1958. Gift of Mr. I. B. Jose, on behalf of the Royal Australasian College of Surgeons.

John Collins Warren. CHURCHILL. To work in the vineyard of surgery, reminiscences of J. C. Warren, 1842-1927. 1958.

Joseph, Lord Lister. GODLEE. Lord Lister, German translation. 1925. Gift of Professor Gilbert Causey.

Autograph Letters

Andrew Douglas, M.D. to *Sir Charles Blagden, M.D., F.R.S.*, 1785. Gift of Mr. C. Robert Rudolf on behalf of the Hunterian Society.

John Hunter to *Mr. Crowfoot*, surgeon, Ipswich. A consultation, without date.

HONORARY FELLOWSHIPS

THE COUNCIL ANNOUNCES that the following have been elected to the Honorary Fellowship of the College:

DAME LILIAN PENSON, Professor of Modern History in the University of London and member of the Committee of Management, Institute of Basic Medical Sciences.

PROFESSOR ADAMS MCCONNELL, of Dublin, Past President, Royal College of Surgeons in Ireland.

MR. E. D. AHERN, of Brisbane, Past President of the Royal Australasian College of Surgeons.

DR. PAUL HAWLEY, of Chicago, Director of the American College of Surgeons.

DR. JOHN H. GIBBON, of Philadelphia, Samuel Gross Professor of Surgery, Jefferson Medical College.

DR. RICHARD LEWISOHN, of New York, Consultant Surgeon to Mt. Sinai Hospital..

APPOINTMENT OF FELLOWS AND MEMBERS TO CONSULTANT POSTS

R. S. MILLER, M.R.C.S., L.R.C.P., D.M.R.D. Consultant Radiologist to Wigan and Leigh Group of Hospitals.

The Editor is always glad to receive details of new appointments obtained by Fellows and Members, either through the Hospital Boards or Direct.

COUNCIL CLUB DINNER, JANUARY 1959

THE JANUARY DINNER was held in the Council Room of the College on Thursday January 8th with Mr. Lionel Norbury in the Chair.

Sir Cecil Wakeley, in proposing the health of the Chairman, said :

" I am so pleased that it has fallen to my lot to propose the health of our Chairman tonight. We have known each other for nearly forty years and our lives have been intersected for a great part. After the first world war I became Lionel Norbury's junior at the Belgrave Hospital for Children and I had a very happy time and no one could have had a better or kinder senior. I suppose Lionel thought my surgery was not too inconsistent or radical for he permitted me to operate on some of his daughters ; and, of course, I do not know a better brace of critics as far as surgery is concerned than Grace and Lionel Norbury. Of course I had just as much confidence in Lionel as a surgeon and he performed a fundamental operation on me in the true St. Mark's fashion.

" Besides our association at the Belgrave we encountered each other at many meetings. Norbury joined the Court of Examiners a year before I did and we served for ten years in those far off and distant days. I joined the Council a year before Norbury, so you see our surgical careers have been a ding-dong affair. While we were on the Court it was the custom for one examiner at each Conjoint examination to entertain the Court at his hospital to luncheon and then perform one or two operations. True to style Norbury performed a colostomy and showed us how to remove piles.

" Of course I always had a certain amount of attraction to Lionel because in the first world war I heard what a distinguished father he had, a well-known Medical Director-General of the Royal Navy, and for his distinguished services this College bestowed the Honorary Fellowship upon him. One thing I could never understand was why Lionel joined the Army and not the Navy in the first world war.

" He obtained his Fellowship in 1907 just three months after Webb-Johnson, Gordon-Taylor, Robert Milne, E. C. Hughes and Gwynne Williams. What a vintage year 1906 was for this College and especially the December examination. Norbury's year, 1907, was no mean year either, for we find Girling Ball, James Walton, Ivor Back, Swift Joly and Leonard Braithwaite all becoming Fellows.

" His association with this College began in 1904 for that was the year he obtained his Conjoint examination. After qualification Norbury had a most distinguished career at St. Thomas's Hospital. He obtained the Cheselden Medal and the Treasurer's Gold Medal and the Beaney Scholarship. Norbury was the last recipient of the special prize which was awarded at St. Thomas's Hospital for general excellence in character and work. He was resident assistant surgeon in 1909 just before Max Page and was also demonstrator in anatomy. It was a time when St. Thomas's had some outstanding men such as Cyril Nitch and Max

Sir Cecil Wakeley proposing the health of Mr. Lionel Norbury.

Page and Adams. He then went off to the first world war and for his distinguished services His Majesty decorated him with the O.B.E.

" Like so many other people who went to the war he found that those who stayed behind had managed to obtain a place at his hospital while he was away. However, he was too nice to be upset by this and the Royal Free Hospital welcomed him with open arms.

" Shortly after this he was appointed to St. Mark's where he certainly had an international reputation and has enjoyed the friendship of countless surgeons both in this country and abroad.

" It is a curious fact that Lionel Norbury was Chairman of this dining club at the January meeting in 1939 and Max Page proposed his health, and now, twenty years later, we are delighted to see him in the Chair again.

" To celebrate your fifty years as a Fellow of this College your colleagues, Lionel, have asked me to present you with this pair of cuff links as a token of their love and affection and with their good will and best wishes."

Mr. Norbury, in replying, said how pleased he was to be in the Chair for a second time, quite an unusual occurrence. He thanked Sir Cecil for all his kind remarks and said he too had thoroughly enjoyed working with him over the years. Mr. Norbury then gave an interesting account of his early years at St. Thomas's, and so ended a very pleasant evening.

A CONSULTATION WITH BOERHAAVE

THE LETTER BOOK of John Arbuthnot, physician to Queen Anne, which forms the first part of the Hunter Baillie collection of autographs in the College Library has recently been restored, the letters being mended and remounted in a fine morocco-bound volume worthy of its priceless contents. These letters are those which Arbuthnot preserved as being of particular interest or by distinguished writers, and they include letters from the leading statesmen and writers of the English Augustan age who were his friends, such as Swift, Pope, Lord Chesterfield and Lord Oxford the Lord Treasurer, or as we should say, Prime Minister. The collection was bought from Arbuthnot's family by William Hunter and descended to his nephew and heir Matthew Baillie, whose descendants in turn gave it to the College more than sixty years ago.

Most of these " literary " letters were printed by G. A. Aitken in his standard *Life and Works of John Arbuthnot* published in 1892. There is one interesting medical letter, however, which has never been published and was not even mentioned by Aitken. This is a Latin consultation by the great Dutch physician Boerhaave on the case of Lord Berkeley, the Lord High Admiral of England. A second letter on the same case belongs to the University of Edinburgh, but our letter seems to be the first advice given by Boerhaave in this consultation.

It is well known that physicians from all over Europe wrote to Boerhaave for advice about their difficulties and many of his consultation-letters have been published. They mostly follow the form of his present letter: a brief general discussion, with directions for treatment, followed by precise prescriptions. Unfortunately in this instance the detailed prescriptions have not been preserved. The following is a translation from Boerhaave's Latin :

H. BOERHAAVE TO THE MOST DISTINGUISHED NOBLE GENTLEMAN AND WISE PHYSICIAN JOHN ARBUTHNOT.

I was much grieved that you were unwell and rejoice that your illness has turned to health. God preserve you safe to old age !

You have been most generous to me in introducing my cousin to the Lord High Admiral of Great Britain and obtaining for him the favour of such a distinguished officer. I offer you my most sincere thanks. I hope he will display honour and courage, to deserve and keep his lordship's valuable favour.

It disturbs me to know that the Right Honourable Earl is the victim of a troublesome illness, but I am relieved by my belief that there is not much danger. It seems to me that the acrid rodent matter of his gouty condition, spread by the blood and hindered from passing the pores of the skin, is fixed there and after injuring the more minute vessels has accumulated under the epidermis ; then if it can once penetrate that, it will escape. I believe that if the infected parts are rubbed two or three times a day with a little of the liquid A warmed, they should then be

covered with the simple plaster B spread all over, and His Excellency should drink an ounce and a half of the draught C every two hours of the day until the inflammation is relieved. Then I advise you to continue with less of the same medicines for a week or two. I write after consideration, to obey the commands of the Distinguished Officer to whom I beg you offer my respect, and I ask you to consider me your obedient servant. Farewell.

Leiden, 30 October, 1725, in the same hour in which I welcomed your letter.

James Berkeley, third Earl of Berkeley, born in 1680, was one of the most distinguished naval officers in the wars with France generally called "Marlborough's wars." After the conclusion of peace by the Treaty of Utrecht in 1712, he was created a Knight of the Garter by King George I in 1718, and appointed Lord High Admiral and Commander in Chief in the Channel in 1719. When the Admiralty was put into commission in 1725 he was made First Lord of the Admiralty as he had previously been from 1717 to 1719. Arbuthnot's and Boerhaave's treatment of his illness seems to have been successful, for he outlived Arbuthnot and did not die till 1736.

W. R. L.

COLLEGE PUBLICATIONS

READERS ARE REMINDED that the following publications issued or sponsored by the College may be obtained from the Editorial Secretary, Royal College of Surgeons of England, Lincoln's Inn Fields, London, W.C.2.

Lives of the Fellows, 1930-1951. By the late Sir D'Arcy Power, K.B.E., F.R.C.S., Honorary Librarian, and continued by W. R. Le Fanu, M.A., Librarian. A single volume, bound in blue cloth, of 889 pages, containing the Lives of all Fellows known to have died between 1930 and 1951. £2 2s. 0d. post free.

A Record of the Years from 1901 *to* 1950. Edited by Sir Ernest Finch, M.D., M.S., F.R.C.S. A slim volume, illustrated, containing a brief history of the College between the centenary and the 150th anniversary of the foundation with lives of all the Presidents since 1900, written by special contributors from their personal knowledge. In red cloth 9s. post free or red paper covers 5s. 6d. post free.

John Hunter, a List of his Books. A short-title bibliography of all known editions of John Hunter's books, compiled by the Librarian. Printed at the Cambridge University Press, and bound in green cloth. 2s. 6d. post free.

A Guide to the Hunterian Museum (*Physiological Series*). This gives a brief account the physiological section of John Hunter's museum, the scope, design and historical value of which is unique. 48 pp. 1s.

A Descriptive and Historical Catalogue of the Darwin Memorial at Down House. Charles Darwin and his family lived at Down House, near Orpington, Kent, for forty-two years and it was here that most of his scientific investigations were made, including his work on the Origin of Species, published in 1859. 33 pp. 1s.

The Portraiture of William Harvey. The Thomas Vicary Lecture for 1948 by Geoffrey Keynes, M.A., M.D., F.R.C.S. With a descriptive catalogue and 33 reproductions of the portraits. £1 5s. 0d.

* *William Clift*. By Jessie Dobson, B.A., M.Sc., Anatomy Curator. A new biography, fully illustrated, of the first Conservator of the Museum at the College. Published by William Heinemann Medical Books Ltd. Bound in blue cloth; 144 pages with frontispiece portrait and 31 plates. 8s. 6d. post free.

* *A separate cheque for this publication would be appreciated.*

SAYINGS OF THE GREAT

" Not only is there an art in knowing a thing, but also a certain art in teaching it." *Cicero.*

" There is nothing which persevering effort and unceasing and diligent care cannot overcome." *Seneca.*

" Perseverance is more efficacious than violence; and many things which cannot be overcome when they stand together, yield themselves up when taken little by little." *Sertorius.*

" Let every man be occupied, and occupied in the highest employment of which his nature is capable, and die with the consciousness that he has done his best." *Sydney Smith.*

Contributions are invited.

DIARY FOR FEBRUARY

Tues. 17	5.00	W. A. H. RUSHTON—Edridge Green Lecture—Visual pigments in the living eye of normal and colour-blind men.*
Thur. 19		D.M.R.D. Examination (Part I), D.M.R.T. Examination (Part I) and D.Phys.Med. Examination (Part II) begin.
	3.45	DR. A. HOWE—Arnott Demonstration—The neurohypophysis—a review of its structure and function.*
	5.00	PROF. A. SORSBY—Ophthalmology Lecture—Retinal aplasia: recessive and dominant forms.*
Fri. 20		Anaesthetic Course ends.
Tues. 24	5.00	DR. R. A. GOODBODY—Erasmus Wilson Demonstration—Repair.*
Wed. 25		Primary F.D.S. Examination and D.T.M. & H. Examination begin.
Thur. 26		D.M.R.D. Examination (Part II) begins.
	5.00	PROF. C. HAVARD—Hunterian Lecture—Non-malignant bile duct obstruction.*

DIARY FOR MARCH

Tues. 3	5.00	PROF. A. J. DAVIES—Hunterian Lecture—Carcinoid tumours (argentaffinomata).*
Wed. 4		D.Orth. Examination begins.
Thur. 5		D.M.R.T. Examination (Part II) begins.
	5.30	MR. ROBERT BRAIN—Otolaryngology Lecture—Oesophageal replacement.*
Tues. 10	3.45	MR. P. C. WILLIAMS—Imperial Cancer Research Fund Lecture—Hormones and Cancer.*
Wed. 11		D.C.H. Examination and First L.D.S. Examination begin.
Thur. 12		First Membership Examination begins.
	2.00	Ordinary Council.
	5.00	PROF. A. G. PARKS—Hunterian Lecture—The microanatomy of the breast.*
Tues. 17	5.00	DR. O. M. SKELTON—Erasmus Wilson Demonstration—Some pathological lesions of the adrenal gland.*
Wed. 18		Board of Faculty of Anaesthetists.
	3.00	Annual General Meeting of Faculty of Anaesthetists.
	4.00	DR. C. LANGTON HEWER—Frederic Hewitt Lecture—Forty years on.*
Thur. 19		Pre-Medical Examination begins.
Fri. 20	5.00	Board of Faculty of Dental Surgery.
Mon. 23	5.00	PROF. A. SORSBY—Ophthalmology Lecture—Irregularly dominant affections of the retina.*
Fri. 27		Good Friday. College closed.
Sat. 28		Last day for applications for Annual Examinerships. College closed.
Mon. 30		Easter Monday. College closed.

* Not part of lecture course.

CHRONIC "BENGAL" SPLENOMEGALY AND ALLIED STATES OF PORTAL HYPERTENSION

Hunterian Lecture delivered at the Royal College of Surgeons of England
on
11th March 1958
by

Professor A. K. Basu, M.S., F.R.C.S., F.A.C.S.
Department of Surgery,
Institute of Post-Graduate Medical Education and Research, Calcutta

THE SUBJECT OF chronic splenomegaly of apparently unknown aetiology has aroused the interest of various workers for well over half a century. Banti in 1894 drew attention to the syndrome of splenomegaly initially associated with fever, anaemia, leucopenia and occasionally with history of haemorrhages. In the subsequent natural history, these cases developed cirrhosis of liver and ascites. This syndrome has since been associated with his name. Osler in 1900 coined the word " splenic anaemia " for this type of case. Warthin (1910) demonstrated evidence of portal hypertension and McNee (1931), in his Lettsomian lecture, spoke about the influence of vascular abnormalities in the pathology of chronic splenomegaly. McMichael (1934) mentioned about two factors in the causation of chronic splenomegaly, viz., portal venous congestion and the factor of hepatitis, which could be responsible for cellular proliferation within the spleen. Larabee (1934) introduced the term " congestive splenomegaly " implying thereby that chronic splenic enlargement was the direct result of portal hypertension. Rousselot (1936 and 1949), while agreeing with this point of view, mentioned that in many cases, the cause of portal hypertension is not identifiable. Thompson, *et al.* (1937) demonstrated consistent rise of portal venous pressure in their operated cases of chronic splenomegaly. Ravenna (1940) agreed about the absence of any demostrable evidence of portal obstruction in many cases and postulated the idea of splenic arterioles being the seat of degenerative changes at an early stage of the disease and this in his opinion was partly responsible for the congestion of the spleen.

Learmonth (1951) recorded a number of cases of " idiopathic " portal hypertension and splenomegaly where no demonstrable block was evident. Hunt (1954) discussed the role of excessive volume of blood as an aetiological factor in this group of cases.

With the recognition of the state of portal hypertension, its means of surgical correction by the various procedures has progressively improved. The works of Whipple (1945), Blakemore and Lord (1945) and Linton (1948) stand pre-eminent in this regard. Significant contributions have also been made by Tanner (1950), Milnes Walker (1952) and Hunt (1954) in England.

Chronic splenomegaly is a common clinical entity in many parts of India, particularly in Bengal. Apart from cases due to known protozoal infections such as malaria or kala-azar, there are a group of cases whose

aetiology and pathogenesis are not apparent even after detailed inves iga. tion. These are the cases which have been given the non-committal erm of " tropical splenomegaly." An approximate idea of the incidenc e of such splenomegalies in different parts of India may be obtained rom the autopsy records of the three big medical college hospitals o the metropolitan cities in India.

TABLE I
AUTOPSY RECORDS OF SPLENOMEGALY

	Total autopsies	Total splenomegalies	" Tropical splenomegaly "
De (1920-1929) .. (Calcutta)	977	528 (54%)	124 (21.7% of all splenomegalies)
Gharpure (1927-1931) (Bombay)	700	280 (40%)	45 (16.1%)
Menon (1899-1933) .. (Madras)	5,034	1,101 (28.8%)	324 (29.2%)

The clinical features of this condition are well known. The majority of the patients come from a lower socio-economic status of life and many of them have lived in endemic malarious areas. The syndrome is

Fig. 1. Picture of a patient with chronic " Bengal " splenomegaly.

characterised initially by a period of intermittent pyrexia—in most cases of malarial origin. After the subsidence of the fever and the control of the protozoal infection, there follows a long course of progressive enlargement of the spleen with chronic ill-health, evidences of hypoprotenaemia, anaemia and even pancytopenia. Most of the spleens extend beyond the umbilicus and some reach the pubis (Figs. 1 and 2).

At a later phase, and unfortunately in the majority of the cases, symptoms and signs of portal hypertension and hepatic dysfunction follow. Some

Fig. 2. The specimen of spleen from the patient in Figure 1. Weight of the spleen, 1,175gm.

have repeated episodes of haemorrhage. Others develop ascites and other symptoms of severe hepatic damage.

De (1932, 1937 and 1939) studied the problem from the autopsy material at the Calcutta Medical College Hospitals and described the histopathological findings. He found atrophy of the Malpighian follicles, thickening of the splenic capsule and prominence of the intrasplenic trabeculae. The sinusoids were dilated and showed erythrophagocytosis. The pulp tissue was poor in cellular elements. He suggested the possibility of an obscure chronic infection of low virulence acting for a long time as being the responsible pathogenic agent and coined the term " Bengal " splenomegaly.

Similar histopathological study was also undertaken by Menon (1934) in Madras. His findings, however, were inconclusive.

In 1938, Menon also conducted an experimental study to determine whether a proliferative reaction can be induced in the spleen by portal congestion and concluded that the so-called Banti's syndrome was not due to blockage of the portal vein. Subsequently he studied the effects on the spleen of well known cirrhosis-inducing agents and suggested that during the development of hepatic cirrhosis there are fibrotic and proliferative reactions in the spleen and also development of definite splenomegaly independent of portal stasis.

Sen Gupta (1943) on the basis of clinical findings considered the cases as the end results of chronic malaria. Chaudhuri (1957) from a study of 134 cases of chronic splenomegaly was of the opinion that, in many of these cases, the initial splenomegaly was malarial in origin. He speaks of

the malarial infection remaining latent and in the absence of sustained antimalarial treatment, the progressive splenic enlargement is an index of the altered host-parasite adjustment and an expression of reticulo-endothelial cell hypoplasia.

We were not convinced that the so-called "tropical" or "Bengal" splenomegaly was a disease entity different from similar types described elsewhere in the world or was peculiar to the tropics. A method of investigation in collaboration between the medical, surgical and histopathological units was therefore planned and seventy-two cases have so far been investigated in detail. These form the basis of this study.

Method of study

In addition to careful scrutiny of their past history, particularly with regard to protozoal infections, jaundice, haematemesis, ascites, etc., and their response to treatment and also examination of their physical state, special investigations were carried out on the following lines :

1. *Haematological*—Examination of the peripheral blood and bone marrow study.

2. *Biochemical*—Examination of plasma proteins and liver function tests.

3. *Radiological*—Oesophagogram and splenoportal venogram (Basu and Das, 1956).

Opportunity was taken at the time of operation to investigate the following :

(*a*) Macroscopic appearances of the spleen, liver and of the portal venous system including presence of collateral venous channels.

(*b*) Estimation of the portal venous pressure.

(*c*) Liver biopsy was taken at operation.

A detailed study of the histology of the spleen and the liver was made from the biopsy material.

These cases, after appropriate operative procedures, were carefully followed up. Their clinical, haemotological and the structural and functional states of the liver were checked up at spaced intervals.

Material

On the basis of the above investigation, the cases could be classified into the following main types :

1. Chronic splenomegaly without evidence of portal hypertension of cirrhosis of liver .. .. 10 cases
2. Chronic splenomegaly associated with cirrhosis of liver and portal hypertension .. .. 41 cases
3. Chronic splenomegaly associated with extrahepatic obstruction.. .. 17 cases
   (*a*) Infrahepatic obstruction—15 cases
   (*b*) Suprahepatic obstruction—2 cases
4. Chronic splenomegaly due to specific diseases .. .. 4 cases

Chronic splenomegaly without evidence of portal hypertension or cirrhosis of liver

This is a controversial group and although we have put down fifteen cases as belonging to this type, the majority of them belonged to an earlier series. There are reasons to think that some of these cases would on close scrutiny, probably, now find place in our second group. This will be evident from the fact that in our last thirty-five cases, there was only one case whom it was considered justifiable to be included in this category.

The size of splenic enlargement in cases in this group is moderate and the progress of enlargement is slow. Associated symptoms of ill health, and manifestation of " hypersplenism " such as anaemia, leucopenia and

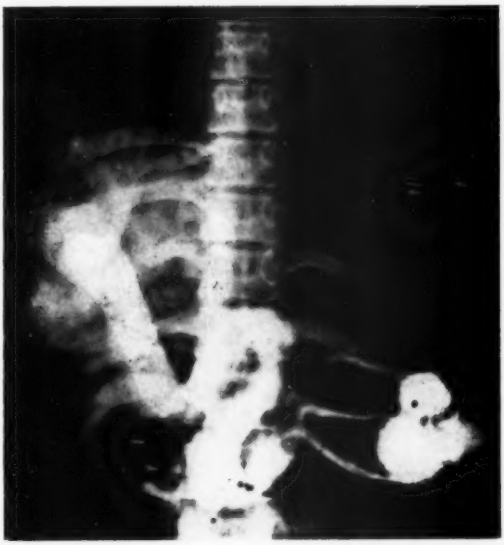


Fig. 3. Splenoportal venography showing dilated and tortuous splenic vein. There are no collaterals. The intrahepatic radicles are ill defined.

thrombocytopenia are mild. There are no histories of haemorrhage. Liver function tests are normal. The splenoportal venography does not show collaterals (Fig. 3). The intrahepatic radicles are ill defined and diffuse. At operation, the spleen is elastic to the touch, is free from adhesions and the liver is normal in appearance and consistency. The portal venous pressure is below 150mm. saline.

The histology of spleen showed marked R.E. hyperplasia of both the white and red pulp without any evidences of vascular congestion (Fig. 4*a*). A brown pigment in macrophage was identified as probably of malarial origin by histochemical tests and optical properties.

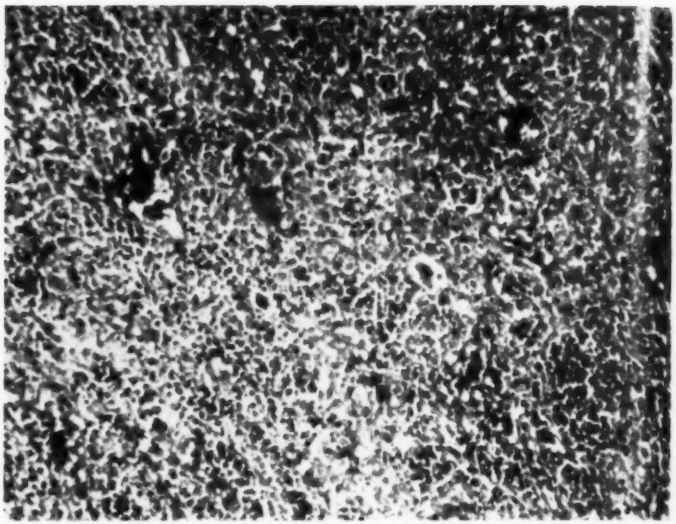


Fig. 4(*a*). Histology of the spleen showing reticuloendothelial cell hyperplasia without much evidence of vascular congestion. H.E. × 220.

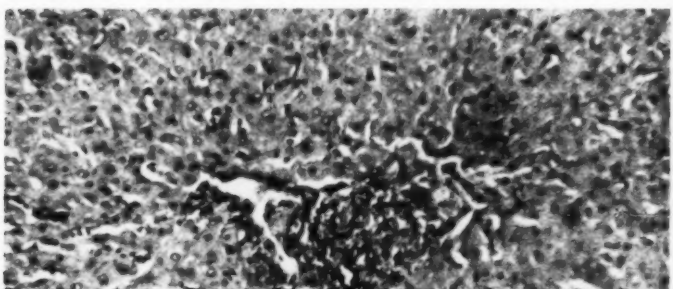
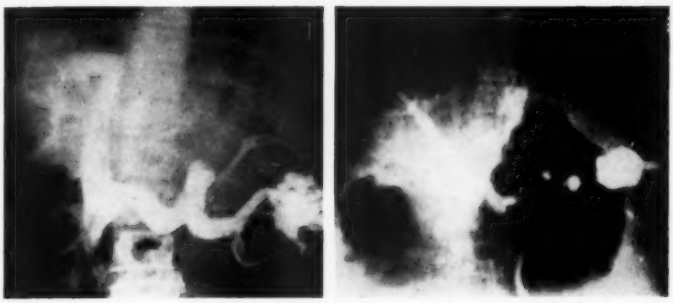


Fig. 4(*b*). Section of liver from a case of reticuloendothelial cell hyperplasia probably of malarial origin, showing infiltration in the portal tract and increase of cellularity in the sinusoids. H.E. × 220.

The liver showed similar reticulo-endothelial hyperplasia—prominent Kupffer cells centering brown pigment and large collection of mononuclear histiocytes in portal tracts (Fig. 4*b*). There was no evidence of any parenchymal cell damage or distortion of the lobular architecture.

Chronic splenomegaly associated with portal hypertension and cirrhosis of liver

This is by far the largest group in our series. The splenic enlargement is progressive and large, often reaching to below the umbilicus. There is chronic ill health and clinical and haematological evidences of " hypersplenism " are marked. In late cases, there may be history of haemorrhages and ascites. Liver function tests show deterioration. Splenoportal



(*a*) (*b*)

Fig. 5(*a*). Splenoportal venography showing well marked collaterals. The splenic and portal vein are dilated and the intrahepatic radicles show truncated appearance.
Fig. 5(*b*). " Withered tree " appearance of the intrahepatic radicles in cirrhosis of liver, well marked collaterals indicating portal hypertension.

venogram demonstrates well marked collaterals—early evidence of portal hypertension even before the appearance of oesophageal varices (Fig. 5*a*). The intrahepatic radicles may show distortion, pooling of the dye, truncating or even the " withered tree " appearance of established cirrhosis (Fig. 5*b*). At operation, there is usually evidence of perisplenitis and adhesions which may be dense and extremely vascular. The splenic vein is extremely dilated and tortuous often exceeding the size of the thumb in diameter. In some cases a well marked thrill can be felt over the splenic artery. The portal venous pressure is well above 200mm. saline. The liver surface in the majority of cases is coarsely nodular and in others there may be fine diffuse granularity and the consistency is firmer than normal.

The splenic histology shows atrophy of the Malpighian corpuscles, dilatation of the sinusoids with thickening of walls (Fig. 6*a*). There was evidence of R.E. cell hyperplasia and in some cases myeloid metaplasia.

The liver showed characteristic histology of post-necrotic cirrhosis

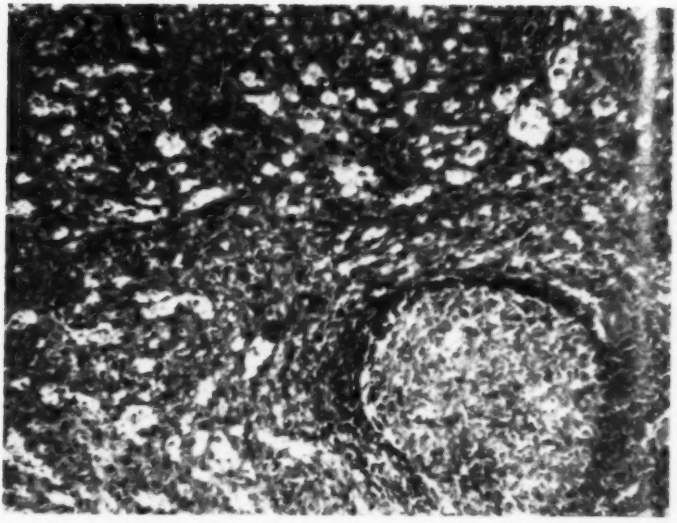


Fig. 6(*a*). Section from spleen of a case of fibro-congestive splenomegaly showing atrophy of Malpighian corpuscle, dilated and thick walled sinusoids. H.E. ×220.

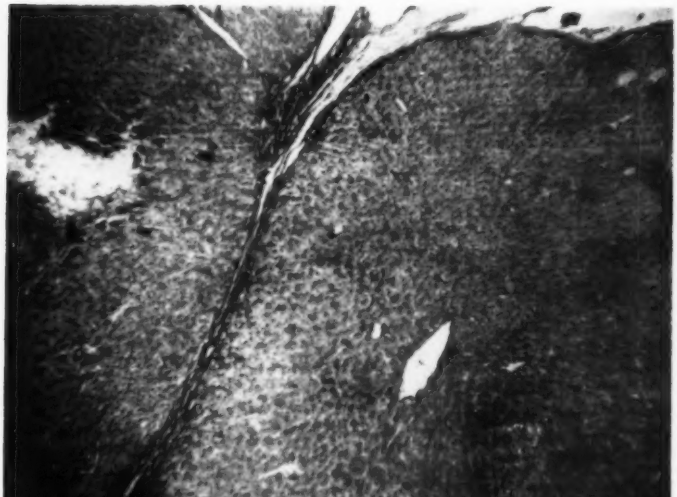


Fig. 6(*b*). Section of liver of post-necrotic cirrhosis showing large nodules separated by connective tissue septa. The individual " pseudolobules " have more than one normal hepatic lobule. H.E. ×36.

in the majority of cases (Fig. 6*b*), diffuse hepatic fibrosis in a smaller number (Fig. 7*a*). Post-necrotic scarring was seen in three cases (Fig. 7*b*).

Chronic splenomegaly associated with extrahepatic obstruction (Das and Basu, 1956)

This formed a fairly sizeable group in our series. There were altogether seventeen cases—in fifteen of which the extrahepatic obstruction was situated proximal to the liver. In other words, the block was infrahepatic.

TABLE II

TYPES OF BLOCK CAUSING PORTAL HYPERTENSION

1. *Infrahepatic obstruction*		15 cases
(*a*) Pancreatic tumour	2 cases	
(*b*) Pancreatitis with fibrosis	4 cases	
(*c*) Portal vein thrombosis	2 cases	
(*d*) Cavernomatous transformation of portal vein	5 cases	
(*e*) Died before operation (cause not definitely known) ..	2 cases	
2. *Suprahepatic obstruction*		2 cases
(*a*) Polycythaemia vera	1 case	
(*b*) Constrictive pericarditis	1 case	
3. *Combined extra and intrahepatic obstruction*		2 cases
(*a*) Cirrhosis + hyperplastic liver nodule	1 case	
(*b*) Cirrhosis + portal vein thrombosis	1 case	

In two cases, the obstruction was confirmed as due to suprahepatic block. In two other cases, the cause of obstruction was both due to intrahepatic and extrahepatic reasons.

The symptomatology of this group of cases is materially different from the previous two groups. Haemorrhage is the predominant symptom. It is repeated and often massive.

One of our patients could predict the approximate date of oncoming haemorrhage. Two of our patients died from massive haemorrhage while waiting for operation. In between episodes of haemorrhage, the patient is fairly normal. History of fever and chronic ill health apart from haemorrhage are not significant. The splenic enlargement is less marked than in other types. Liver function studies show no abnormality. Splenoportal venography can accurately delineate the site of obstruction and often gives an idea of its nature. At operation, the anatomical abnormality of the portal venous system and the nature of the obstructive agent can usually be determined with accuracy. Portal venous pressure shows high figures.

The liver, except in suprahepatic obstruction cases, is usually normal in appearance and to the touch. Histology of the spleen shows evidences of congestion. Liver histology is normal.

The nature of the obstructive agents in our cases is listed in Table II. Four cases were due to the splenic vein being enveloped by fibrosis associated with chronic fibrosing pancreatitis. Three of these cases were diagnosed at operation and in the fourth case, who unfortunately succumbed to a severe episode of haemorrhage prior to operation, the obstruction was confirmed at autopsy by passing a fine catheter into the splenic vein. This got obstructed at the exact site previously noted in the

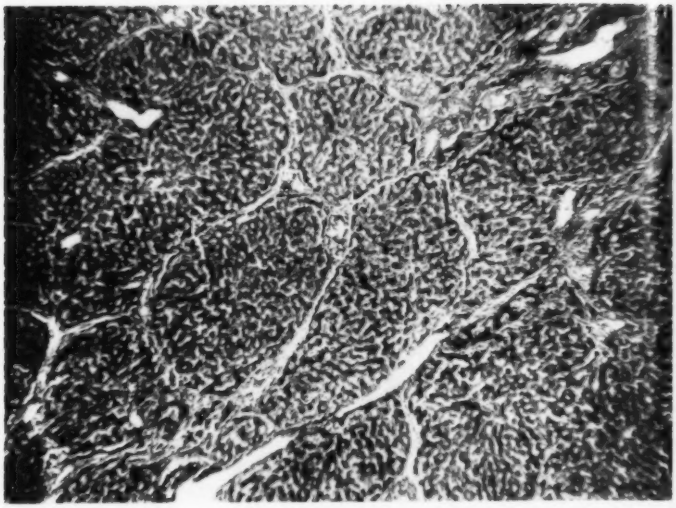


Fig. 7(*a*). Section of liver from a case of diffuse hepatic fibrosis showing small uniform pseudolobules in which the normal relationship of portal tract and efferent vein have been completely lost. H.E. ×120.

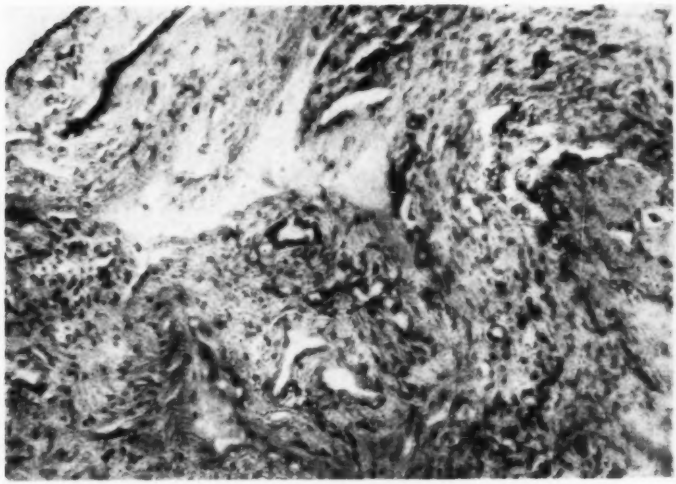
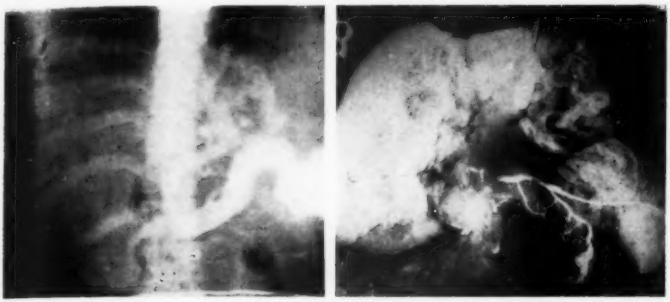


Fig. 7(*b*). Section through a wide scar from a case of post-necrotic scarring showing collagenous connective tissue with proliferating bile ducts. The liver from the surrounding large lobules showed a normal architecture. H.E. ×220.

splenoportal venogram during life (Fig. 8*a*) and the radio-opaque dye introduced through this tube did not pass beyond this site (Fig. 8*b*).

There were two cases of splenic vein obstruction due to tumour of the pancreas. In one case, it was possible to do partial pancreatectomy

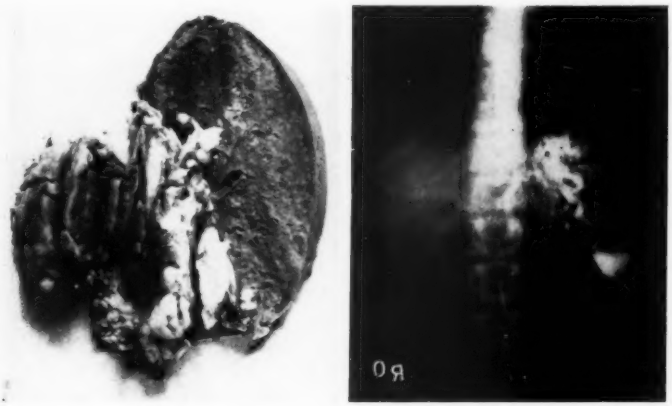


(*a*) (*b*)

Fig. 8(*a*). Splenoportal venography showing extrahepatic block with well marked collaterals.

Fig. 8(*b*). Autopsy study showing the obstruction of the catheter in the splenic vein by fibrosing pancreatitis.

together with splenectomy and ligation and division of the large tortuous veins draining towards the fundus of the stomach (Fig. 9*a*). The venogram of this patient was highly interesting (Fig. 9*b*).

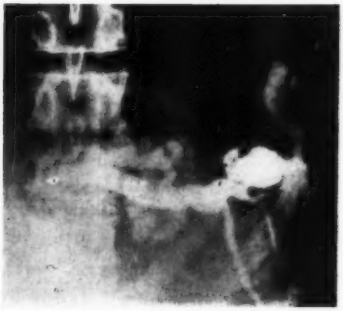


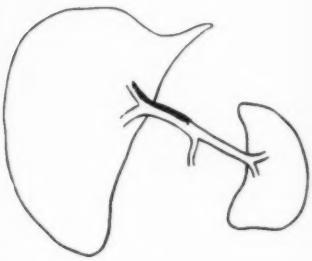
(*a*) (*b*)

Fig. 9(*a*). Picture showing a tumour in the tail of the pancreas obstructing the splenic vein.

Fig. 9(*b*). Splenoportal venography showing diversion of the splenic effluent through the short gastric veins to the fundus of the stomach.

There were two cases of thrombosis of portal vein. In one case the diagnosis was suggested by venography (Fig. 10*a*). Both were confirmed at operation. One case was associated with advanced cirrhosis of liver. She died seven days after operation due to progressive hepatic failure and at autopsy dissection the thrombus was seen to completely occlude





(*a*) (*b*)

Fig. 10(*a*). Splenoportal venography showing obstruction at the origin of the portal vein due to portal vein thrombosis. Numerous collaterals are present.
Fig. 10(*b*). Diagram showing a large thrombus in the portal vein occluding the left branch completely.

the left branch of the portal vein and extend downwards to the main trunk and tail off at the junction of the superior mesenteric and splenic vein. A fairly patent channel was going to the right branch (Fig. 10*b*).

There were five cases of cavernomatous transformation of the portal

(*a*) (*b*)

Fig. 11(*a*). Splenoportal venography in a case of cavernomatous transformation of portal vein with numerous tortuous collaterals.
Fig. 11(*b*). Splenoportal venography in suprahepatic obstruction showing well marked delineation of the intrahepatic radicles up to the periphery. Collaterals are present.

vein. Instead of the normal large portal vein, there were multiple tortuous tributaries of smaller calibre enveloping the right border of the lesser omentum. Three of these cases could be demonstrated prior to operation by splenoportal venography (Fig. 11*a*).

Of the suprahepatic obstruction group, one was a case of polycythaemia vera, where histology of the liver biopsy material showed evidences of hepatic venous tributary occlusion. The other was a case of constrictive pericarditis where pericardectomy relieved the portal hypertension. Both these cases demonstrated the pattern of venogram, which we have associated with suprahepatic obstruction (Fig. 11*b*), viz., well marked delineation of the intrahepatic radicles right up to the periphery of the liver with their normal dichotomous branching and distribution together with presence of collaterals in the portal venous system.

Chronic splenomegaly due to specific causes

Four of these cases were referred to us for surgery and were operated on. Two were cases of resistant type of kala-azar where, in spite of repeated and prolonged specific treatment, there was recrudescence of infection. Splenomegaly and symptoms of hypersplenism were marked. There were no evidences of portal hypertension. It was postulated that the backwaters of enlarged splenic sinusoids were the storehouse of the L.D. bodies which thereby escaped the onslaught of the specific drugs. Splenectomy in both these cases had apparently cut short the vicious circle and led to marked and long term improvement in health. The other two cases were congenital haemolytic anaemias of Cooley's type and splenectomy was undertaken for recurrent attacks of haemolytic crisis. One was operated on four years ago and continues to do well. The other was operated on recently.

There were no episodes of haemorrhage in these cases. Liver function tests except for rise of globulin fraction in kala-azar cases were normal. The spleen was free from adhesions and mobile and splenectomy was an easy process. Portal venous pressure was low and the liver was normal in appearance and to touch.

DISCUSSION

Chronic progressive splenomegaly associated with hepatic fibrosis is perhaps not uncommon in many parts of the world. However, the type of gigantic splenomegaly which usually reaches beyond the umbilicus and sometimes reaches the pubis is perhaps more common in our part of India than elsewhere. The initial cause of most of these splenomegalies is probably due to malarial infection. This is supported by many indirect evidences. Most of the patients come from endemic malarial areas; there is history of fever of malarial type in many cases. Successful anti-malarial measures have substantially reduced the incidence of such splenomegalies. In the early stage of the disease, anti-malarial treatment may cause subsidence of the splenomegaly (Chaudhuri, 1957). However,

at the time when these patients present themselves for treatment, no direct evidence of malarial infection is discoverable either in the haematological or bone marrow study or in the histology of the resected spleen. The reason or reasons for the progressive enlargement of the spleen have until now not been definitely understood or appreciated.

Our study shows that in nearly all such splenomegalies, there is evidence of congestive changes in the splenic parenchyma associated with greater or lesser degrees of fibrosis. This is evidenced by the large size of the splenic vein and its intrasplenic radicles, the dense tortuous vascular adhesions that anchor the spleen to its surrounding structures, the oozing out of massive quantities of blood with visible shrinkage of the spleen after splenectomy and the enormous dilatation of the splenic sinusoids and peri-arterial haemorrhages seen on histology. The significance of the thrill which is often palpable over the trunk of the splenic artery in these cases is not yet fully understood, but no doubt it indicates a state of hyperactive circulation through the splenic artery and arterioles. This thrill is immediately abolished by clamping the artery at the hilum or after splenectomy, lending support to the view that the reason for the hyperactive circulation lies within the splenic substance. It is possible that the enormous sinus dilatation brings about direct communications between the arterioles and the sinusoids—in effect a state of intrasplenic arterio-venous aneurysm, thus explaining the presence of the thrill over the artery.

We have rarely come across a case belonging to this type where instead of these fibro-congestive changes, the splenomegaly was due mainly to pure reticuloendothelial cell hyperplasia. There is record of only one such case in our series. In such cases, macroscopical evidences of congestion as described before are also absent.

Our records also show that nearly all these large splenomegalies are associated with certain degrees of hepatic fibrosis with considerable distortion of the liver parenchyma. As mentioned before, the histological changes in the liver conform mainly to those of post necrotic cirrhosis with nodular hyperplasia, although in some cases diffuse hepatic fibrosis of the Laënnec type has also been found.

In addition, definite evidence of portal hypertension as measured by a saline manometer at operation has been found in the majority of the cases.

These findings are at some variance with the observations made by previous workers on the subject of "Bengal" splenomegaly, viz., De (1937), De and Tribedi (1939), Menon (1934), Napier (1939), Sen Gupta (1943) and Chaudhuri (1957). The histological pictures described by De differ in some respects from those described by British, European and American investigators of allied types of splenomegalies in that the evidence of intrasplenic haemorrhages and its consequences were not present in his cases. In addition, De believed that the progressive enlargement of the spleen with the associated symptoms was due to a low grade infection of

a chronic nature. Chaudhuri (1957) has postulated the idea of latent malarial infection remaining in a subactive phase indefinitely and stimulating the reticuloendothelial cells in the spleen. He does, however, concede that " the proof of their malarial origin is not unequivocal and further investigation may show that some of them are of idiopathic origin or due to some other cause such as virus infection like infective ' hepatitis', brucellosis and schistosomiasis (not reported in India)."

From the study of our material, it appears to us that the so-called " Bengal " or " tropical " splenomegaly is another example of " fibro-congestive splenomegaly " the like of which is also found in other parts of the world. Whatever be the initial cause of splenomegaly and in Bengal particularly, the question of malarial infestation seems most plausible in many cases—the subsequent progressive increase in the size of the spleen is, in our opinion, secondary to the hepatic fibrosis—in other words an example of intrahepatic portal obstruction. The causes of the intrahepatic damage may be various. The role of the spleen itself in elaborating a possible toxic substance that might damage the liver has been mentioned by McNee (1931) and also by Pemberton and Kiernan (1945) but does not seem to us to be entirely credible. We have had many examples of chronic splenomegaly due to specific causes, such as the haemolytic anaemias or due to mechanical infrahepatic type of obstruction where the liver parenchyma does not show any evidence of fibrosis even after a long time. We believe that the splenomegaly itself has little or no role in the initiation of the fibrotic process in the liver. We believe also that the hepatic pathology is primary in origin but once the hepatic damage has occurred and the consequent fibrotic process is well established, the large hypertrophied spleen continues to exert an adverse effect resulting in the persistence and progressive increase of the fibrotic process in the liver. This it probably does by the enormous increase of the splenic effluent which side-tracks the more important venous return from the intestinal tract and thereby further injures the already struggling cells of the hepatic parenchyma. There is therefore a vicious circle involved in the whole process.

One factor needs consideration and that is the size and weight of the spleen. It is curious that the spleen should attain such gigantic sizes in our cases considering that the size of the spleen in our extrahepatic obstruction group has been relatively small. McMichael (1934) was of the opinion that portal obstruction *per se* is unlikely to produce splenic enlargement of more than three times its normal size. The normal weight of the spleen varies from 150 to 200gms. In intrahepatic obstruction, therefore, splenic enlargement should not exceed 600gms. in weight whereas our spleens often exceeded 1,500gms. This is explained by the fact that the fibro-congestive " Bengal " splenomegaly is not a primary splenomegaly, but is secondary to a previously hypertrophied spleen probably of malarial origin.

Episodes of haemorrhage were less frequent and also less severe in this type of splenomegaly. In contrast, in our infrahepatic obstruction group, the incidence of haemorrhage was almost invariable and was also of massive proportions. Two of our fifteen infrahepatic obstruction group of cases died from repeated exsanguinating haemorrhage before surgical help was possible, whereas none of the forty-nine intrahepatic obstruction group died from haemorrhagic complications. This had a bearing on our surgical management in that splenectomy was considered a sufficient operation in a large number of cases.

We tried to ascertain the role of portal venous pressure in the causation of haemorrhagic episodes. This was done in twenty-six consecutive cases and the results are interesting.

TABLE III

PORTAL VENOUS PRESSURE AND HAEMORRHAGIC EPISODES

Portal venous pressure as measured at operation

201-300mm. saline	10 cases
301-400mm. saline	11 cases
401-500mm. saline	4 cases
Above 500mm. saline	1 case
Portal venous pressure of less than 300mm. saline—bled	5 cases
Portal venous pressure of over 300mm. saline did not bleed	6 cases
Portal venous pressure of over 400mm. saline did not bleed	2 cases

It appears to us, therefore, that there is no coincidental relation between portal venous pressure and haemorrhagic episodes, which depend also to a large extent on the site of the block and the distribution of the abnormal collaterals.

The question of idiopathic or " essential " portal hypertension has been mentioned by some observers, viz., Rousselot (1936), Ravenna (1940) and others. Hunt (1954) spoke about the possibility of excessive volume of splenic effluent being responsible for portal hypertension in the absence of demonstrable obstruction. It seems to us that, although evidences of obstruction may not be demonstrable by clinical or radiological methods or at operation, in many cases of splenomegaly where the portal venous pressure as measured at operation shows high values, histological examination of the liver parenchyma in such cases usually shows evidences of distortion of lobular architecture due to fibrosis.

We are therefore inclined to think that portal hypertension, associated with congestive type of splenomegaly, is usually an indication of obstruction in the portal venous system which may only be evident on careful histologic studies of the liver.

We were impressed by the large numbers of cases in our series where the obstruction was due to extrahepatic causes. Five cases of cavernoma of the portal vein proved to us that this abnormality may not be as rare as is usually supposed. Obstruction of the splenic vein by a fibrous envelope resulting from chronic pancreatitis was next in order of frequency, followed by portal vein thrombosis and tumours involving the pancreas. It is evident that the role of this method of obstruction in the causation of

portal hypertension was not fully appreciated until recent years. As is to be expected, the liver parenchyma in cases of infrahepatic obstruction is usually normal both on naked eye appearance as well as histologically.

The operative approach either to the shunt operation or even to splenectomy in the large splenomegalies is now a standardised procedure in our hands. There is no question that the combined abdomino-thoracic approach and the division of the diaphragm give incomparably better exposure and ensure division of the large adhesions containing tortuous vascular channels either with the under surface of the diaphragm or within the posterior layer of the lienorenal ligament with precision and deliberation. The types of operations performed in our series are shown in Table IV.

TABLE IV
TYPES OF OPERATIONS PERFORMED

1. Splenectomy alone	49 cases
2. Splenectomy with splenorenal shunt	12 cases
3. Portacaval shunt	2 cases
4. Ligation of hepatic and splenic artery	6 cases
5. Ligation of splenic artery alone	1 case
	70 cases

In six cases splenorenal shunt was attempted but had to be abandoned due to technical difficulties and the operation ended as splenectomy. In one case of attempted portacaval shunt operation could not be done due to abnormality of the portal vein. Two cases died before operation.

The specific role of splenectomy alone in the management of portal hypertension has been debated and it has been stated that the surgeon who in cases of portal hypertension is doing splenectomy alone and not combining it with a shunt procedure is not doing the best possible thing for his patient (Linton, 1948). That is probably true in the type of cases where large splenomegaly is not the most important factor and where there are episodes of repeated haemorrhages. In the type of splenomegalies with which we have dealt, however, the enormous size of the spleen with evidences of progressive hypersplenism is the most important consideration. Haemorrhagic episodes in this group were infrequent and insignificant. In such cases, we have contented ourselves with doing splenectomy alone. The value of splenectomy in this group lies in the cutting off of the large volume of splenic effluent and therefore of the large portal hypervolaemia. We have made some preliminary efforts in the volumetric determination of the actual amount of splenic effluent in these cases. Our preliminary studies show that this amount at least exceeds 600 cc. per minute.

Where history of haemorrhages is significant, the shunt procedure was considered imperative and we have done this on fourteen occasions—twelve splenorenal and two portacaval. In addition, in seven cases the shunt procedure was attempted but could not be performed due to

technical difficulties or due to the anatomical abnormality of veins. We maintain that although the portacaval shunt is a technically easier procedure, splenorenal shunt with splenectomy is the operation of choice in the type of cases that we meet with. We would reserve portacaval shunt for the post-splenectomy or for the post-splenorenal shunt bleeder and also for the type of cases where splenomegaly is not significant but where there is repeated history of haemorrhages.

We have performed a few ligation operations according to the concepts of Reinoff (1951) and Berman, *et al.* (1951). These, however, have been done only in late cases of hepatic damage associated with marked ascites and also in the absence of haemorrhages. The results of these operations in our hands, however, have been disappointing.

RESULTS OF OPERATIONS

The results of our operations are summarised in Tables V, VI and VII.

TABLE V
FOLLOW-UP OF CASES

Group	Up to 1 yr.	1-2 yrs.	2-3 yrs.	3-4 yrs.	4-5 yrs.	5-6 yrs.	Remarks
I Chronic splenomegaly without cirrhosis of liver and portal hypertention—10 cases	1	2	2	0	0	0	4 lost in follow-up 1 died (operative)
II Chronic splenomegaly associated with cirrhosis of liver and post hypertension—41 cases	11	13	6	1	1	0	5 lost in follow-up 2 operative deaths 2 died after operation 1 two months after 1 after one year
III Chronic splenomegaly with extrahepatic obstruction							
Intrahepatic obstruction—15 cases	4	3	3	1	0	0	2 died before operation 2 died after operation
Suprahepatic obstruction—2 cases	1	1					
IV Chronic splenomegaly due to specific causes—4 cases	1	1	2				

TABLE VI
RESULTS OF OPERATIONS

1. Splenorenal shunt		12 cases
Mortality	Nil	
Recurrence of haemorrhage	2 cases	
Doing well (6 months to 4 years)	10 cases	
2. Porta caval shunt		2 cases
Both doing well (1 year and 2 months)		
3. Splenectomy done for haemorrhage cases (where shunt failed due to technical reasons)		7 cases
Recurrence of haemorrhage in 2 cases		

TABLE VII
RESULTS OF OPERATIONS

Death before operation	2 cases
Operative mortality	3 cases
Known deaths after operation	4 cases
Lost in follow-up	9 cases

OVERALL FOLLOW-UP OF CASES

54 cases have been followed up for periods varying from 6 months to 6 years.

Clinical condition	1.	46 cases are doing well
	2.	5 cases have had recurrence of haemorrhage.
	3.	3 cases have developed ascites (they did not have ascites prior to operation).
Repeated haematology study ..		36 cases have improved as compared to pre-operative status.
Repeated liver function study .. (done in 31 cases)		26 cases show improvement as compared to pre-operative status.
Repeated liver biopsy study .. (done in 18 cases)		12 cases show improvement as compared to pre-operative status.

In addition to regular clinical check-up of the patients, we have been doing repeated haematological, liver function and liver biopsy studies of our cases at three or four monthly intervals. This study is continuing and we hope in another paper to be able to present a detailed review of the state of liver function and of liver pathology of these cases in addition to their haematological and clinical status. However, from a review of our follow-up material, it is even now clear that in the large majority of our cases, the operation has been well worth-while. Of the total of fifty-four cases followed up from six months to six years, forty-six cases are clinically doing well ; five cases have had recurrence of haemorrhage and three have developed ascites. The haematological status has markedly improved in

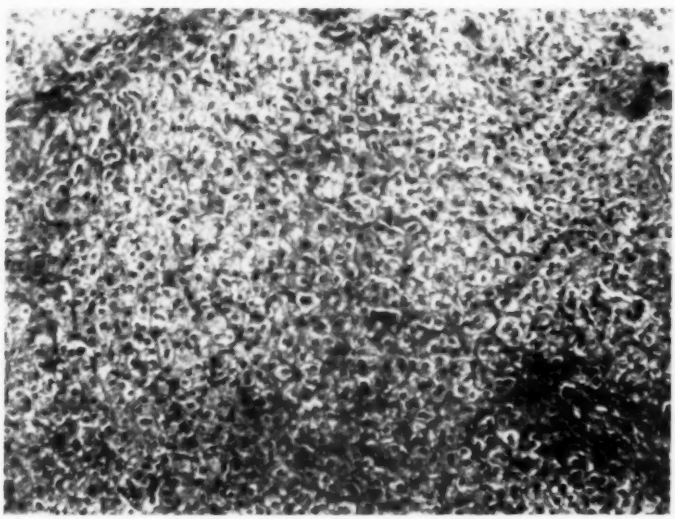


Fig. 12. Section of a liver from a follow-up case of a post-necrotic cirrhosis eight months after splenectomy showing mild scarring. H.E. × 220.

the majority indicating elimination of the factor of hypersplenism. Liver function and liver biopsy studies show improvement in fair proportion.

We have been trying to analyse the effect of splenectomy on the histology of the liver in those cases where cirrhosis was already present prior to operation. The overall results are not yet clear but in at least some of the cases, we have been impressed by positive functional as well as structural improvement of the liver parenchyma indicating the arrest and reversibility of the fibrotic process in the liver and the elimination of the possible injurious influence of the hyperplastic spleen (Fig. 12). This improvement in the liver function is usually associated with noticeable enlargement of its size indicating activity of the regeneration process.

In summary, therefore, it seems that unless the fibrotic process in the liver has led to irreversible hepatic damage, the operation of splenectomy does bring about a state of overall improvement in the patient.

Among our shunt operations, there has been as yet no operative or post-operative mortality but two cases have had recurrence of haemorrhage. In one of these, subsequent portacaval shunt performed over a year ago has stopped further episodes of haemorrhage.

There were seven cases where a planned shunt procedure for haemorrhagic attacks could not be completed due to anatomical abnormalities of veins or due to technical difficulties and the operation ended as a splenectomy. Two of the cases have bled—one two years and another one and a half years after the operation. Five remain as yet without haemorrhage and in two of them, the post-operative period has exceeded four years.

SUMMARY AND CONCLUSION

I have attempted to review and highlight the problem of the large chronic splenomegaly which abounds in certain parts of India and particularly in Bengal. The pathogenesis and the management of this condition until now have not been made clear and a rather confused literature has grown around it. In the absence of a specific nomenclature, the appellation " Bengal " splenomegaly was attached to it and it appeared to some observers as a specific entity different from allied conditions met with elsewhere in the world.

It appears from a review of our material that the so-called " Bengal " splenomegaly is a chronic fibro-congestive splenomegaly associated with and secondary to intrahepatic type of portal bed block and grafted on a spleen which initially might have enlarged due to malarial infestations. Such splenomegalies are usually associated with moderate increase of portal venous pressure and the liver parenchyma shows evidence of a fibrotic process which is progressive. Haemorrhagic episodes are relatively uncommon in this type and their main problem is chronic ill-health with hypersplenic syndrome manifestations. They should be operated on early and, in the absence of already existing irreversible hepatic damage, should lead to long term good results. The operative risk is small.

These cases should be differentiated from splenomegalies due to extrahepatic obstruction which seems to be relatively common. Here

haemorrhagic manifestations are frequent, often dangerous and the splenomegaly is smaller in size. Splenectomy with or without a shunt procedure should lead to complete cessation of symptoms in these cases.

A few other interesting observations from our findings may be recapitulated. There is no exact coincidental relationship between portal venous pressure and the incidence of haemorrhage which depends also on the site and the type of obstruction.

Idiopathic or " essential " portal hypertension probably does not exist or must be extremely rare. In the absence of a demonstrable or obvious block, some evidence of structural damage and fibrosis in the liver can usually be found.

The commonest type of liver damage met with in this type of splenomegaly is post-necrotic cirrhosis with nodular hyperplasia. It has been suggested that the splenomegaly *per se* is not responsible for the initiation of the hepatic damage. However, there are reasons to think that once the liver damage is established, the splenomegaly is to some extent responsible for its persistence and progress culminating in hepatic failure. Operations undertaken at this late stage are likely to be unsuccessful.

ACKNOWLEDGMENTS

I am indebted to a large number of people who have helped me in this work. It would be invidious to mention some names rather than others but two colleagues, the late Professor A. Das and Professor B. K. Aikat, have contributed a great deal to the study of this problem, and the work and the views expressed herein should be looked upon as having been jointly performed and jointly held by us. I am also grateful to Professor S. Bose for help in radiology and to Dr. R. N. Chaudhuri, Director, School of Tropical Medicine, Calcutta, for referring many cases to me for operation.

REFERENCES

BANTI, G. (1894) *Sem. med.* (*Paris*) **14**, 381.
BASU, A. K., and DAS, A. (1956) *Brit. med. J.* **2**, 916.
BERMAN, J. K., MULLER, L. P. FISCH, C., and MARTZ, W. (1951) *Arch. Surg.* (*Chicago*) **63**, 623.
BLAKEMORE, A. H., and LORD, J. W. (1945) *J. Amer. med. Ass.* **127**, 685.
CHAUDHURI, R. N. (1957) *J. Indian med. Assn.* **28**, 101.
DAS, A., and BASU, A. K. (1956) *Brit. med. J.* **1**, 325.
DE, M. N. (1932) *Indian J. med. Res.* **19**, 1029.
————(1937) *Rep. Sci. Adv. Board Indian Res. Fund Ass.*, p. 92, New Delhi.
————and TRIBEDI, B. P. (1939) *Indian med. Gaz.* **74**, 9.
GHORPURE, G. (1933) *Indian med. Gaz.* **68**, 35.
HUNT, A. (1954) *Proc. Roy. Soc. Med.* **47**, 469.
LARABEE, R. C. (1934) *Amer. J. med. Sci.* **188**, 745.
LEARMONTH, J. (1951) *Brit. med. J.* **2**, 67.
LINTON, R. R. (1948) *New Engl. J. Med.* **238**, 723.
MCMICHAEL, J. (1934) *J. Path. Bact.* **39**, 481.
MCNEE, J. W. (1931) *Lancet* **1**, 951.
MENON, B. (1934) *Indian J. med. Res.* **19**, 565.
————(1938) *J. Path. Bact.* **46**, 357.

NAPIER, L. E. (1939) *Indian med. Gaz.* **74**, 1.
OSLER, W. (1900) *Amer. J. med. Sci.* **119**, 54.
PEMBERTON, J. DE J., and KIERNAN, P. (1945) *S. Clin. North America*, **25**, 880.
RAVENNA, P. (1940) *Arch. intern. Med.* **66**, 879.
REINOFF, W. F. (1951) *Bull. Johns Hopk. Hosp.* **88**, 368.
ROUSSELOT, L. M. (1936) *J. Amer. med. Ass.* **107**, 1788.
——————(1949) *J. Amer. med. Ass.* **140**, 282.
SEN GUPTA, P. C. (1943) *Indian med. Gaz.* **78**, 255.
TANNER, N. C. (1950) *Proc. Roy. Soc. Med.* **43**, 147.
THOMPSON, W. P., CAUGHEY, J. L., WHIPPLE, A. O., and ROUSSELOT, L. M. (1937) *J. clin. Invest.* **16**, 571.
WALKER, R. M. (1952) *Lancet* **1**, 729.
WARTHEN, A. (1910) *Int. Clin.* **4**, 189.
WHIPPLE, A. O. (1945) *Ann. Surg.* **122**, 449.

SIR HARRY PLATT, Bt.

DURING HIS RECENT tour of India and Ceylon, which was sponsored by the British Council, Sir Harry Platt delivered a message of greeting from the President of the Royal College of Surgeons of England, Sir James Paterson Ross, to the members of the Association of Surgeons of India at the Annual Meeting held in Vizakhapatnam (December 27th to December 31st 1958). At the meeting Sir Harry read a paper on " Malignant Tumours of Bone," gave the first Kini Memorial Lecture, and was elected an Honorary Member of the Association.

DONATIONS

DURING THE LAST month the following generous donations have been received :

Restoration Fund:

£3,000 Mathilda Marks Kennedy Charitable Trust (further gift).

Appeal Fund:

£5,000 (plus £3,695 13s. 0d. tax to be recovered). Finnamore Trustees (for Mr. B. M. Mavroleon).

£1,000 Prudential Assurance Company.

£500 Sir Max Page, K.B.E., C.B., D.S.O., F.R.C.S.

£100 Trustees of the Rt. Hon. Baron Austin of Longbridge (further donation).

£54 7s. 6d. Sale of gifts from Mr. W. R. Gibson, F.R.C.S.

£10 10s. 0d. Mr. R. E. Norrish, F.R.C.S.

Faculty of Dental Surgery:

£50 Prudential Assurance Company.

RECENT OVERSEAS VISITORS TO THE COLLEGE

RECENT OVERSEAS VISITORS to the College have included Professor Adams A. McConnell of Dublin and Dr. Richard Lewisohn of New York, both of whom received the Honorary Fellowship of the College at the meeting of Council in February. An account of the ceremony will be published in the April issue of the Annals.

THE HAZARDS OF URETERO-INTESTINAL ANASTOMOSIS

Hunterian Lecture delivered at the Royal College of Surgeons of England
on
25th March 1958
by

John Hopewell, F.R.C.S.
Surgeon, Royal Free Hospital

"Ah, Doctor, life is a mystery, which you vainly endeavour to penetrate! . . . Let us cease to grope our way blind-fold, and trust to nature; that is much better."—NAPOLEON BONAPARTE, quoted by F. Antommarchi.

THESE WORDS OF the Emperor Napoleon, quoted by his physician Antommarchi, were spoken within a few months of his death from a growth of the stomach in May 1821. They sound as a clear call to the pursuit of the experimental method in unravelling the problems of disease, and as such I would like to take them to introduce a study of the effects of urinary diversion. But in their true context they may be thought even more pertinent to this subject, for they were in fact a cry for some respite from the rigours of treatment. Against those well-intentioned but gruelling prescriptions that were the fashion of the day, the enema and the emetic, the blister and the purge, that master of strategy was unable to deploy an adequate defence, though he tried every ruse of the sick-room in the attempt. He had no palate for medicine. While noting that some acquired a taste for it, he was prepared to swallow it only if convinced of the need. Now to carry conviction, treatment must confer benefit in due proportion to the hazards of its administration. It is our duty to strike this balance before we prescribe. The patient cannot and should not be expected to do so, for, despite the spread of medical education to the parlour as a form of light entertainment, he has not the evidence on which to judge for himself, as did the Emperor Napoleon. That clear intellect, which had revised the social systems of a continent, was well equipped to do so. His judgment, though phrased in commendable good humour, was devastating: "Doctor, if I am to die, I should like to die of disease."

Some such consideration is apposite to the subject of urinary diversion, for the hazards it sets are formidable enough to demand careful reckoning against any advantage it may bestow. In youth, that is for certain congenital defects, the balance is sufficiently in its favour for it to be an acceptable method of treatment. To review this point, Harvard and Thompson (1951) quoted Dr. C. H. Mayo, who gave his opinion that some two-thirds of patients with untreated exstrophy of the bladder die before reaching their twentieth year. In following the cases treated by ureterocolic anastomosis at the Mayo Clinic since 1912, they found the expectation of survival to be increased by one-third. It seems likely that the outlook for patients treated in later decades may be further improved. It is

interesting to note that the longest survivors of this operation for exstrophy of the bladder, reported by Stevens (1941) and Cordonnier and Sojut (1957), were alive forty-three and thirty-eight years, respectively, after the operation. Upon the striking contrast, however, in the results for older patients undergoing uretero-colostomy, comment has ever been made. After allowance for the shorter natural expectation, and the grave nature of the diseases demanding diversion in later years, it seems apparent that it promises a shorter term of survival and a greater chance of complications than in the young. The outlook is particularly unfavourable for patients with growths of the bladder. In recent years we have turned more to irradiation, from an interstitial or remote source, as more nearly fulfilling our criterion of wise treatment. Yet despite such reservation, it seems sure that attempts to perfect a method of urinary diversion will proceed in the decades ahead. The surgical endeavours of the first fifty years of this century are likely to be remembered for their mastery of the problems of excisional surgery. Already there is promise that its second half will see advances of equal note in the surgery of restoration. Urology is an old specialty. It is one of those branches that budded early from the main stem of general surgery, the scope of a special instrument marking out its limits, and, some would add, its limitations. Yet it maintains a virile growth over this new field of reconstructive surgery. Successful operations have been performed to restore or replace every organ of the urinary tract. A dominant fashion has been the use of part of the bowel, isolated or intact. This vicarious duty of the intestine has posed problems still unsolved. These may be considered thus:

1. *Surgical Anatomy and Operative Surgery*
   (*a*) Choice of intestinal segment.
   (*b*) Technique of uretero-intestinal anastomosis.
2. *Surgical Physiology*
   The biochemical disturbances:
   Nature: Uraemia and acidosis.
   Hyperchloraemia.
   Depletion of potassium and calcium.
   Causes
   Adaptive responses

1. SURGICAL ANATOMY AND OPERATIVE SURGERY

From about the time of the outbreak of the First World War to the end of the second, ureteric transplantation into the intact colon was respected as the established route of urinary diversion. Earlier pioneers had tried various procedures, all in turn abandoned as impractical. For some three decades only the surgical nonconformist attempted the occasional use of any method other than uretero-sigmoidostomy with the safety of its almost aseptic technique. Even so, this was an acceptance by default rather than acclaim. In their valuable review published in 1936, Hinman

and Weyrauch voted the advantage in theory and practice to submucous colonic implantation, but found no method safe from the complications of sepsis and obstruction. Almost as they wrote, however, sulphonamides introduced the help of chemotherapy against infection, and the attendant advances in surgery allowed confidence for new endeavours. The neglected experiments of the past were privileged to a retrial, and for some the verdict was reversed. This pattern is a recurring one in surgical history and reminds us that an innovation must be not only well conceived, but timely (Fig. 1).

Tizzoni and Foggi (1888), in their experimental preparation, drained both ureters into an isolated ileal loop with its distal end anastomosed to the posterior urethra. Bricker (1950) and Merscheimer, *et al.* (1950) reintroduced the use of the ileal segment, draining to an abdominal stoma (Fig. 1). Couvelaire (1951) and Pyrah (1956) have used a modification of the earlier and more ambitious concept of restoring urethral drainage and sphincteric control. The isolated terminal ileum and caecum of Verhoogen (1908), drained by appendicostomy, has again been on trial by Cortes (1946) and Powell (1949); whilst Bricker (1950) recorded drainage by caecostomy (Fig. 1). The caecum has also been used for bladder substitution but with the opposite direction of urinary flow, so that the ileocaecal valve might confer a degree of continence (Gilchrist, Merricks, Hamlin and Reiger, 1950). An isolated sigmoid segment has been tried by Bisgard, experimentally in 1943, and clinically in 1948. Further investigation of its value was reported as an experimental study by Rubin in 1949. Mauclaire (1895) made animal preparations with the isolated recto-sigmoid bladder. He established an iliac colostomy, whilst suggesting that in clinical cases a perineal colostomy through the fibres of levator ani could be used (Fig. 1). In 1898, Gersuny proposed the restoration of faecal continence with the rectosigmoid bladder by bringing the sigmoid colostomy stoma to the perineum within the fibres of the anal sphincter (Fig. 1). In recent years the principle of Mauclaire has been reintroduced into clinical practice, notably by Kinman, *et al.* (1953) and Pyrah (1957). In 1955, Lowsley and Johnson reported the successful use of Gersuny's anal persphincteric colostomy, of which there was a further report by Johnson in 1956.

Of all these methods, two are chiefly on clinical trial at the present time, the isolated ileal segment and the recto-sigmoid bladder. It is still early to evaluate their merits in relation to each other and to uretero-sigmoidostomy. Experience teaches, but she is tutor rather than coach. She gives no notice of her classes, and her lessons are often confused. At the moment her most diligent pupils would interpret her teaching for us in this way:

1. The isolated ileal segment

Bladder replacement by an isolated ileal segment minimises the effects of back pressure and ascending infection in the urinary tract. It does so

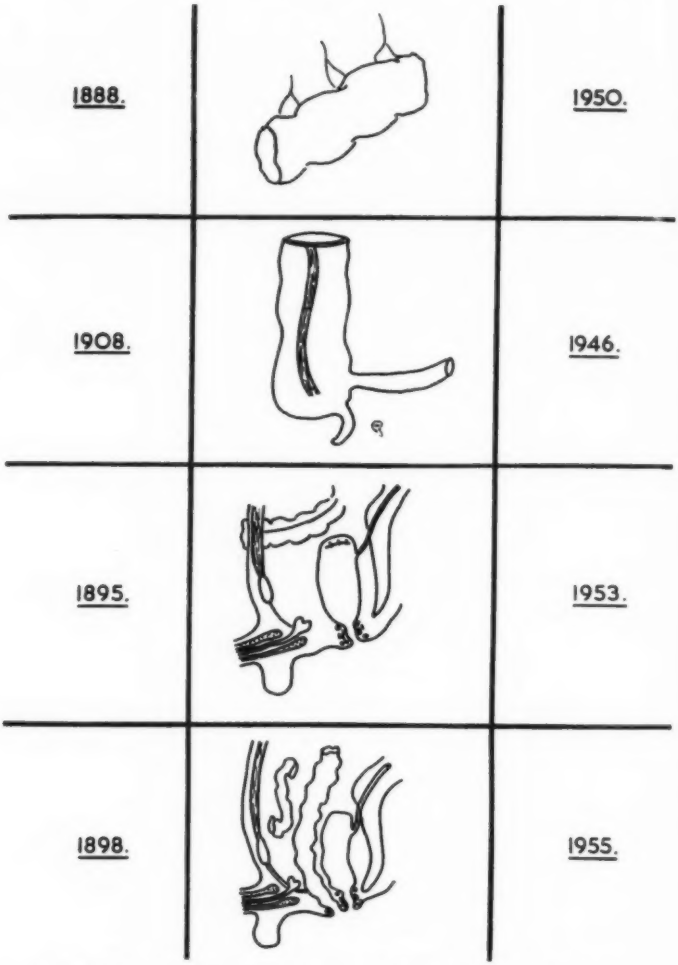


Fig. 1. History of bladder replacement by isolated intestinal segment.

at the expense of urinary continence, and at some risk of post-operative complications. In the collected series reported by Wells (1956) for the British Association of Urological Surgeons, the operative mortality was as high as 30 per cent., and 120 of 209 cases had some complication, notably ileus, fistula, mechanical obstruction and burst abdomen. There have also been records of prolapse and stenosis at the stoma.

2. Isolated recto-sigmoid segment

This affords a satisfactory and continent urinary reservoir, separate from the faecal stream, and with a voiding pressure considerably lower than that of the intact rectosigmoid (Smith and Hinman, 1955). Nevertheless, the interference with normal function of an unaffected system has delayed its wide adoption. The method of Mauclaire involves an iliac colostomy. Gersuny's concept is brilliant but involves a considerable dissection, be it noted, along the path described by Belt, *et al.* (1939) for his perineal prostatectomy. The upper cut end of the sigmoid colon is brought down in front of the rectum, downwards within the perimeter of part of the anal sphincter, to open on the perineum just anterior to the anus. Now this route is described as being between the internal and external parts of the anal sphincter, but I appreciate from Dr. Belt's demonstrations and my own dissections, that it is in fact within the wide ring that we recognise as the subcutaneous part of the external sphincter, between this and its superficial and deep parts.

3. The intact colon

The urinary continence which it confers, together with minimal interference with the alimentary tract, explain the favoured position of this method. However, biochemical disturbances have been reported in as many as four out of five cases and of these, many suffer ill-health of varying degree. Moreover, the high pressures in the normal colon are transmitted to the kidney with deleterious effect. Herein lies the challenge to devise an anastomosis to rival the quiet efficiency of the uretero-vesical orifice.

(*b*) *Technique of uretero-intestinal anastomosis.*—John Simon first performed urinary diversion in 1851, by establishing a fistulous track between each ureter and the rectum. Half a century passed before the appearance of a more formal technique of transplantation, that based on Witzel's (1891) principle of gastrostomy. This was well named the "muscularizing principle" by Hinman and Weyrauch, who wryly note that it has been attributed to native invention in the United States (Martin, 1900), France (Depage and Mayer, 1904), Russia (Tichoff, 1908) and England (Stiles, 1911). When in 1911 the versatile Coffey adapted his submucous method of choledocho-duodenostomy to the new field, its advantage was at once apparent. I believe though that attention should be given to Vermooten's (1934) conclusion that its virtue lay in the security it offered from leakage and infection, rather than in any valvular action that it might bestow. Indeed, no indirect method, as we classify these, consistently achieves the precise balance of tissue forces which offers that tantalising reward, an efficient sphincter. The disappointment of stricture formation has inclined more recent workers to disdain such attempts, and fashion a wide direct anastomosis between ureter and bowel, without pretentions to valve action, but at least assuring free

urinary drainage (Nesbit, 1949 ; Cordonnier, 1949). Wyland Leadbetter (1951), however, retains an intramural tunnel that on experimental evidence and in his experience confers an advantage. Thus, until recently might we have summarized the situation, echoing Hinman and Weyrauch's uncharacteristically gloomy comment, " It would seem that every surgical principle imaginable has been tried." That it had not was shown in 1953 by Willard Goodwin, who introduced the principle of transluminal anastomosis. Enticed by the advantages of a direct approach, he relied on chemotherapy to sterilise the bowel, and opened it through a longitudinal antimesenteric incision (Fig. 2). Passing an instrument across the

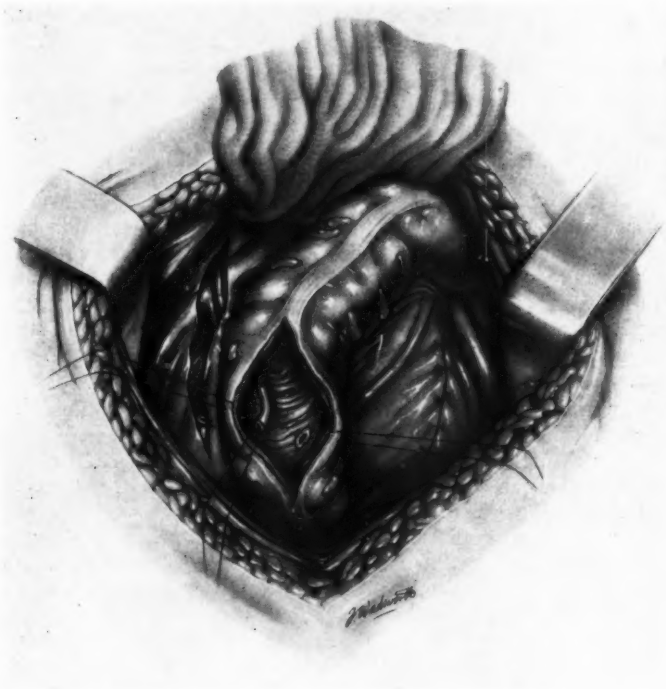


Fig. 2. Goodwin's transluminal method of uretero-colic anastomosis.

lumen, he pierced the posterior wall and drew the ureters straight forward into the colon. This allows a precision formerly unknown in anastomosis, in adjusting the tension of the ureter, and its course through the bowel wall. Those who prefer a valve or cuff enjoy perfect conditions for its tailoring. The route of the ureters through the mesentery to the colon is

valued by Denis Browne in his method. This development by which they pierce the posterial wall of the colon seems the most appropriate arrangement. It allows secure anastomosis with a shorter stump of ureter than other methods and confers a natural mobility to the colon after operation.*

2. PHYSIOLOGICAL ADJUSTMENT TO TRANSPLANTATION

Whatever interest we may devote to the anatomical restoration, as much must be given to the physiological adjustment which it may entail. This response is still by no means fully defined or understood. An epitome of current views is afforded in the excellent survey by Stamey (1956) of electrolyte imbalance in uretero-sigmoidostomy. He reminds us that Boyd first described acidosis in 1931, yet twenty years elapsed before Ferris and Odel (1950) noted its high incidence and also its correction by colonic lavage, pointing to chloride absorption as its cause. This suggestion was elegantly confirmed by Parsons and his associates (1952) at Leeds. Yet not all patients developed hyperchloraemia, and not all of those who did so had acidosis. Lapides (1951) from his observations following urine enemata, believed that its incidence depended upon a renal tubular defect. It would indeed offer a welcome encouragement to the surgeon to perfect a method of anastomosis, if the undamaged kidney were spared this complication. But Stamey has confirmed that instillation of urine into the colon in the normal subject can bring about a hyperchloraemic acidosis. He continues to review the evidence that uretero-sigmoidostomy affords the opportunity for hypokalaemia. Potassium may be lost both from cellular dehydration as a result of hyperchloraemia, and by secretion into the lumen of the bowel from the colonic mucosa. He comments that potassium depletion alone causes renal damage, yet its restoration under these circumstances, where other factors are adversely affecting renal function would itself be dangerous. Severe calcium depletion may also occur. He concluded that the operation of uretero-sigmoidostomy should probably be abandoned. So much is widely appreciated, and yet the operation still enjoys the regard of many, perhaps most, surgeons. It has been shown that control of the potassium imbalance is a practical possibility (Pyrah, 1954). Moreover, the record of forty years' survival is a proud one. Its very possibility engenders a cautious optimism and I should like to bring forward some evidence that it is justified.

Samuel Butler described the body as but a pair of pincers over a bellows and a stewpan, the whole mounted upon stilts. The simplicity of this account of human physiology is to be welcomed, but I cannot condone its neglect of renal function. We should take care to avoid the same error in considering the effects of urinary diversion.

If these may be so severe as to bring the advisability of uretero-sigmoidostomy into question, it must be inferred that in those patients

* A short film, taken at laparotomy for second stage radical operation for carcinoma of the vulva, six weeks after ureteric transplantation by this method, was shown to demonstrate the mobility of the colon.

surviving the procedure for long periods in full health, a very considerable adaptation must have occurred. The experimental studies related to this response are strikingly consistent in their witness to the importance of the renal contribution. In brief summary I would classify these experimental findings under :

(*a*) General changes.

(*b*) The biochemical disturbance.

(*c*) Morbid anatomy of the kidney.

(*a*) General changes

There is a loss of weight, which is subsequently regained (Geer and Dragstedt, 1938 ; Boyce, 1951). Fluid intake and output is increased, up to four- or five-fold (Boyce, 1951) (Fig. 3).

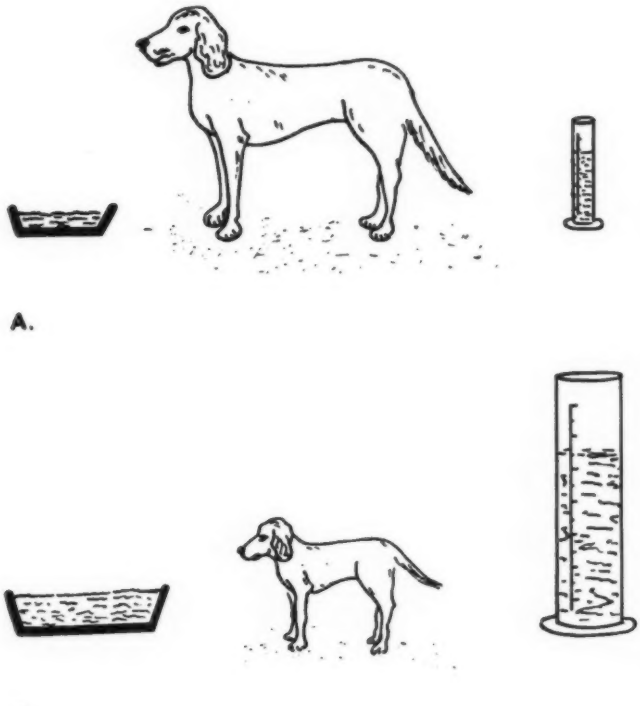


Fig. 3. Fluid balance and weight changes.

(*b*) **The biochemical disturbance**

Transplantation of both ureters into the duodenum resulted in almost complete reabsorption of the urine, with rise of non-protein nitrogen to very high levels, depression of CO_2 combining power, and death from uraemia in a few days (Baird, Scott and Spencer, 1917; Kingo Goto, 1918; Hinman and Belt, 1922) (Fig. 4*a*).

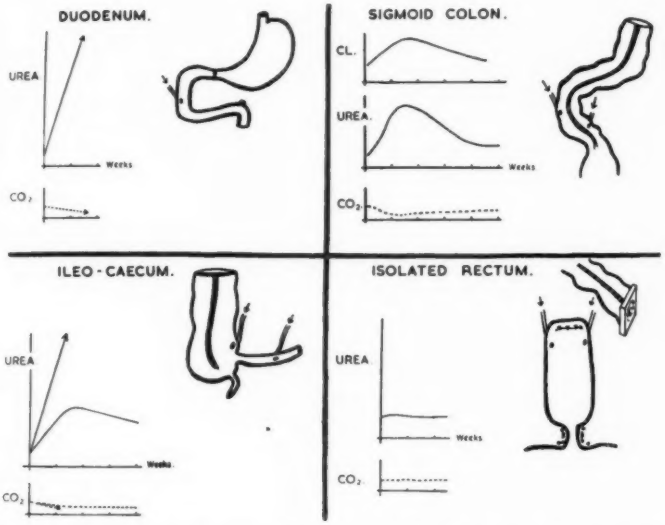


Fig. 4. Effects of urinary diversion into different levels of the intact intestinal tract.

Diversion of all the urine into the ileo-caecal region (Fig. 4*b*) may result similarly in death after ten to twelve days, with the same biochemical disturbance (Boyce, 1951); though Geer and Dragstedt (1938) showed that survival was possible for relatively long periods, despite a raised blood urea and depressed CO_2 combining power. When urine is diverted into the intact colon (Fig. 4*c*), there is a rise of blood urea in the weeks after operation, followed by a fall almost to normal levels (Bollman and Mann, 1927; Boyce, 1951). CO_2 combining power is simultaneously depressed and there is some elevation of serum chlorides. Hartman in 1933 devised five methods of causing slow reabsorption of urine in the experimental animal; notably by side-to-side anastomosis of the bladder to the free limb of a Roux-en-Y loop of small intestine, and by cutaneous jejunostomy into which he could instil urine or its constituents (Fig. 5). The identity of the changes resulting from these two methods—again a rise of blood urea and depression of CO_2 combining power—demonstrated most elegantly that the effects of transplantation were due to reabsorption

of urinary constituents from the bowel rather than a primary renal failure. He further noted that with repeated instillations of urine, the animal would tolerate ever increasing amounts, until finally it would survive the administration of a volume certainly lethal for a normal dog. He concluded that there had been an adaptive change in the kidney as a result of the increased excretory work imposed upon it. In his studies on diversion of urine into the intact colon, performed under exemplary conditions of measurement and control, Boyce was particularly interested in the return

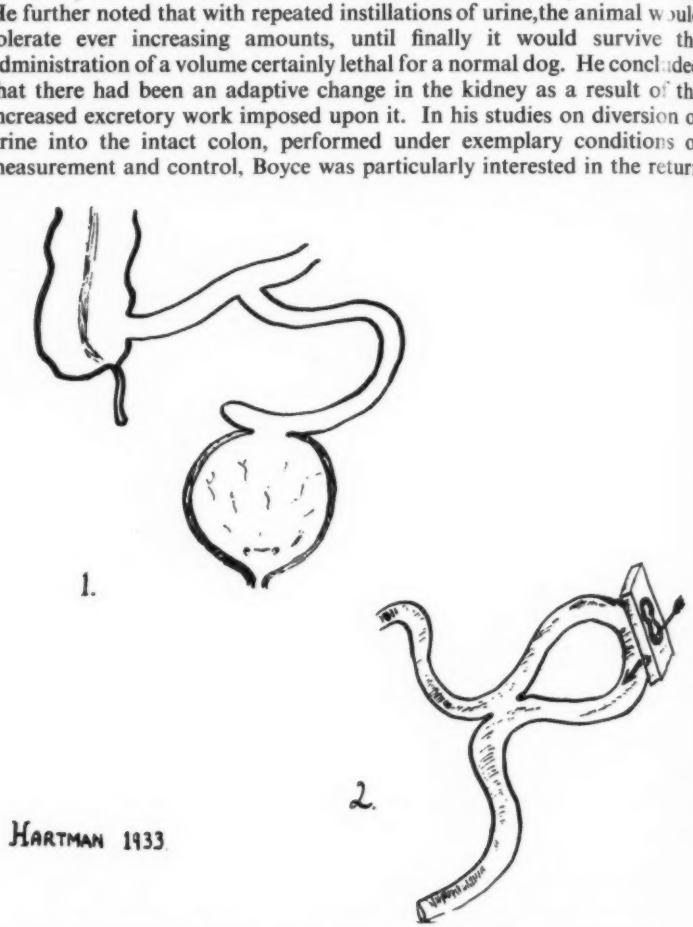


Fig. 5. Hartman's experiments on slow absorption of urinary constituents.

of blood levels to almost normal values in the surviving animals. He again drew our attention to this as evidence of a real increase in renal excretory effort, called out in response to an increased load. In confirmation of this view he diverted the urine into the isolated rectum, from which absorption would be expected to be minimal, and noted the absence of any significant variation of blood levels from the normal (Fig. 4*d*).

(*c*) **Morbid anatomy of the kidney**

Further evidence for the concept of renal response is given by the striking structural changes, seen at post-mortem examination of kidneys that have been subjected to an increased excretory load. This response is one of hypertrophy, associated with increased vascularity causing glomerular congestion, and changes in the cells of the tubular epithelium. Whilst staining normally, as many as four to six of these in a single high-power field are seen to be undergoing mitosis (Fig. 6). Hinman and Belt (1922, 1923) stressed the importance of these changes and demonstrated the similarity to those of compensatory hypertrophy after nephrectomy. Hartman in 1933 noted that they were brought about equally by urinary diversion and by instillation of urine or its constituents into the intestine. At the same time he drew attention to a simultaneous destructive effect

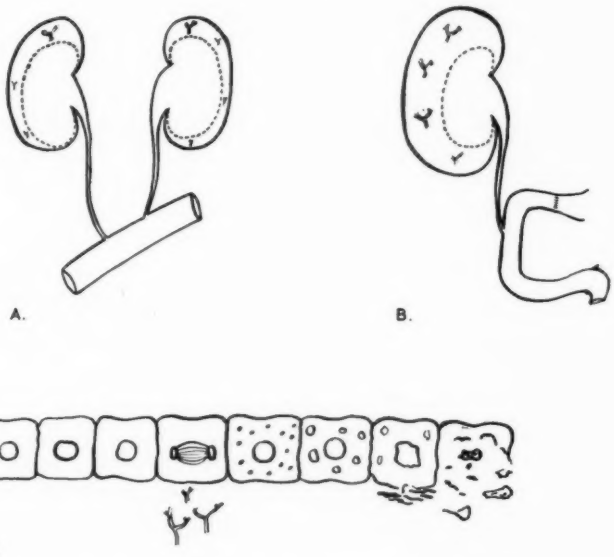


Fig. 6. Changes in the kidney following absorption of urinary constituents.

upon the tubular epithelium, characterised by granular and vacuolar degeneration, desquamation and even disintegration of its component cells. He further contrasted these findings with Newburgh's (1919) observations on increased protein intake. In 1935, Bollman and Mann again demonstrated the striking acceleration in the rate of compensatory hypertrophy of the remaining kidney after unilateral nephrectomy, when its ureter was implanted into the duodenum. Increases of 60 to 100 per

cent. were seen, remarkably enough, within nine days of the operation. After sigmoid diversion, Boyce (1951) noted an increase in total renal weight to nearly double that of a control group of dogs.

To continue this chain of investigation the first requirement seemed to be a study of the effects of the passage of urine through an isolated ileal loop, a preparation by now in clinical use. Irvine, *et al.* (1956) had made investigations of this problem, but his interest lay in possible late biochemical disturbances, and my proposal was to watch the immediate post-operative effects for comparison with the earlier studies I have described.

To draw some sort of base-line for my study I repeated the observations on diversion into the intact colon made by Boyce. My preparations were uretero-colic anastomosis rather than vesico-colic as his, but the findings were of parallel changes. Then diverting the urine into the isolated rectum, I noted again the absence of biochemical disturbances.

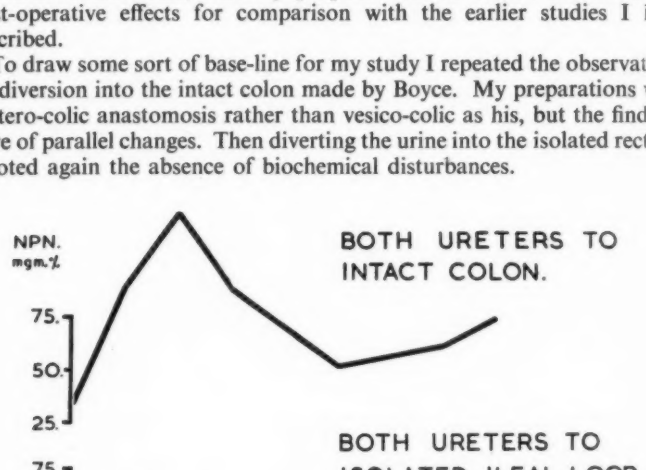


Fig. 7. Comparison of absorption from intestinal segments.

My first studies on the isolated ileal loop were made in collaboration with Professor Frank Hinman, Jr., when working as an affiliate in the Department of Urology in the University of California Medical Center, San Francisco, under Professor D. R. Smith. Investigation of blood levels showed a rise of blood urea and depression of carbon dioxide combining power, with some slight rise of blood chloride. These then returned to normal. The preparations used could be criticised as being ureteric implantations, so that some deleterious effect upon the kidney from the anastomosis could contribute to the results. I therefore repeated this experiment at the Buckston Browne Farm, anastomosing the dome of the bladder to the isolated loop after division of the urethra. The findings were again the same, except that no significant rise of chloride was seen. This enabled us to compare, in the experimental animal, the effects of diversion into those segments of the intestine now commonly used in clinical practice (Fig. 7). It does demonstrate the possibility of absorption effects with the isolated loop, though these are small compared with those from the intact colon. By contrast, no changes are seen when the isolated rectum is used as an artificial bladder.*

It is not my intention to draw any conclusion from these results about the comparative behaviour of the ileal segment and the recto-sigmoid bladder in surgical practice. It appeared to me, however, that the value of this preparation in experimental work, once it had been noted that measurable changes followed its use, was the facility it afforded for the study of the whole physiological problem set by the passage of urine through the intestine. All the classical experiments pointed to the likelihood of the changes induced being proportional to the surface area of absorptive mucosa involved. Yet this had never been directly proved, for the observations were made on different portions of the bowel, with varying capacity for absorption, and with varying rates of passage of urine through them; this particularly in the colon, by reason of the controlling effects of the ileocaecal valve and anal sphincter, and the occurrence of reverse peristalsis.

I therefore prepared animals with isolated loops of increasing length, with the bladder base anastomosed to their proximal end, and draining distally through an abdominal stoma. As a control I demonstrated the absence of blood changes following mobilisation of two isolated ileal segments through which no urine was draining. Three dogs (Nos. 24, 25, 30) were then prepared, of weights 8 kg., 7 kg. and 7 kg., and with ileal segments of 3 in., 9 in. and 12 in. length respectively. The changes in the first were the same as those noted above for the ileal loop, a slight rise in blood urea and depression of CO_2 combining power, which returned to normal levels (Fig. 8). The second animal showed a steady rise of

* I would emphasise that these experimental findings are those following diversion into the isolated *rectum*. In clinical practice an isolated recto-sigmoid segment has been used. This includes as much as half of the sigmoid loop (Pyrah, 1957), and therefore a measurable degree of reabsorption has been noted in studies of this preparation.

blood urea over a period of six weeks, followed by a gradual fall, finally after ten weeks to just within normal limits. CO_2 combining power fell below normal (Fig. 9). Just after this its blood urea rose and it died suddenly without evident cause. I would note, moreover, that this animal

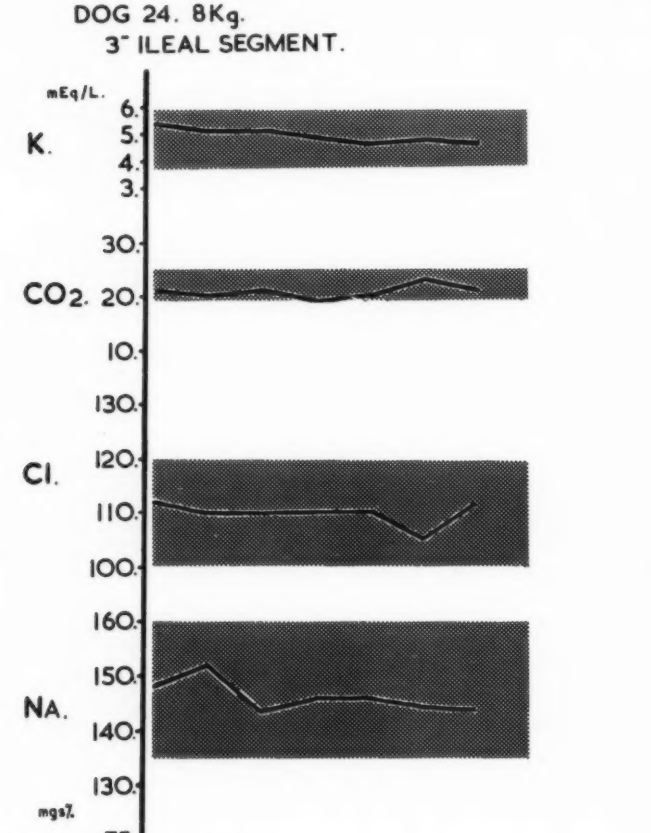


Fig. 8. Absorption from 3 in. ileal segment.

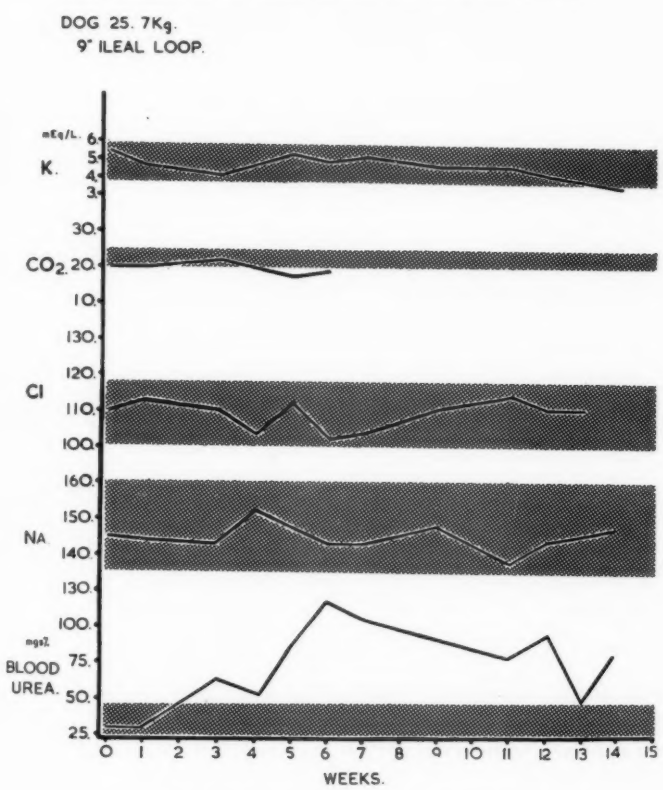


Fig. 9. Absorption from 9 in. ileal segment.

appeared to lose flesh during the first weeks after operation, when the blood urea was rising, was noted as losing weight, and drank and put out an abnormally high volume of fluid. During the period of recovery, it gained weight and filled out, though not to its previous size. The third animal with a 12 ins. segment, rapidly lost weight, and drank copiously after operation. The blood urea rose steadily to 565 mg. per cent. before death on the tenth day. CO_2 combining power fell very low, ultimately to 6 m.Eq. During this time, however, the sodium and chloride did not move outside their normal range, whilst the serum potassium rose by only 0.2 m.Eq. above the upper limit of normal just before death (Fig. 10).

At autopsy, the first dog being killed, no abnormality outside the renal tract was seen, though the second dog was somewhat wasted, while the third showed evidence of gross dehydration. The urinary tract of each

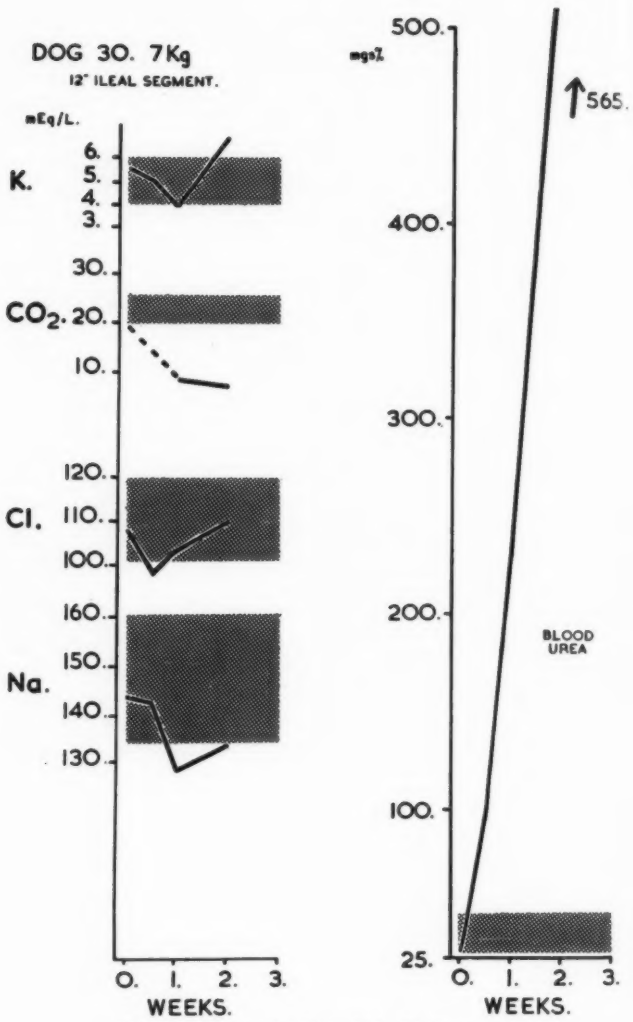


Fig. 10. Absorption from 12 in. ileal segment.

animal was examined.* Figure 11 shows the typical naked eye appearance. The kidney substance was a little bulky. There was no evidence of back-pressure or infection in renal pelvis or ureters of dogs 24 and 30. One

* By Dr. Keith Elliott, Consultant Pathologist to the Brighton and Lewes Hospital Group, to whom I am particularly grateful both for his enthusiastic cooperation and his expert comment upon this somewhat unusual material.

side of dog 25 showed mild hydronephrosis. On histological examination there were no changes to suggest that death could have resulted from renal damage, though some glomerular congestion was reported, and also degenerative changes in the epithelium of the tubules.

Fig. 11. Post-mortem specimen, ileal segment preparation.

I believe this experiment must be taken as proof that the reabsorption of its constituents is directly proportional to the area of the mucosa over which the urine passes. Moreover, that such reabsorption of normal constituents is sufficient to result in death with uraemia and acidosis,

without significant change in sodium, chloride or potassium levels. This is in accord with the observation of Atchley and Benedict (1927) that in uraemia from experimental ligation of the ureters, chloride and HCO_3 are usually lowered, while phosphate and sulphate levels correspondingly rise.

Any attempt to calculate from these figures what might be the longest segment of ileum for safe use in man would be too inaccurate to be of any value, but I am sure it is greater than any likely to be used in clinical practice.

I would prefer to turn your attention next to the very important issues related to the reverse slope or phase of recovery marked by the return of blood urea to normal levels in those animals surviving the first effects of urinary reabsorption. It might, of course, indicate a reduced rate of absorption from the bowel and such an adaptive change might be thought not beyond the power of the intestinal mucosa when we consider the marked response to the need for increased absorption seen in those rare cases of massive resection of small bowel (Flint, 1912). To check this I set up a simple perfusion experiment, in which I ran a solution of urea through a loop of intestine that had been used as a urinary conduit, and also through another loop of small bowel of equal length, from the same animal—this is an acute experiment. The rate of absorption of urea was the same in each. Simple as this experiment was, and without proper controls, its findings discouraged further investigation of reduced reabsorption as a cause of the considerable compensatory effort that must be involved. I felt persuaded to investigate the renal response for which much evidence has been given by former studies.

It seemed that the isolated ileal segment at last provided a means of measuring renal function before and after diversion. Clearance estimations depend upon accurate and complete collection of urine over timed periods, and this presents an almost impossible task with drainage into the intact bowel. Collection from an isolated ileal segment, however, seemed a practical possibility, and was therefore undertaken in collaboration with Dr. A. A. G. Lewis.* Tests were carried out on the unanaesthetised fasting animals, which were on a standard diet. Clearance of creatinine, urea and P.A.H. was estimated over three fifteen-minute periods, after which the maximum tubular excretion of P.A.H. was estimated over a ten-minute period. In the first animal (Dora, 36, 9 kg.) whose results I present, urine was collected from the bladder before operation by urethral catheter. At operation I then diverted all the urine through a $4\frac{1}{2}$ ins. isolated ileal segment. The biochemical changes followed the familiar pattern for an ileal segment of this length. Our clearance tests carried out before and in the weeks after operation enabled us to follow

* Here I must express my indebtedness to Dr. Lewis, who gave me not only his special help in the biochemical laboratory at the Buckston Browne Farm, but even more his instruction and assistance in the performance and interpretation of the clearance tests.

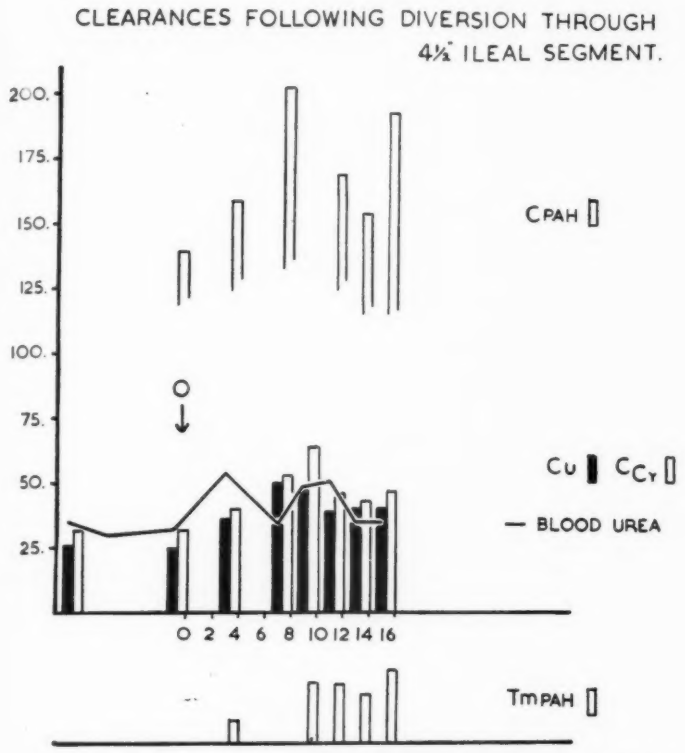


Fig. 12. Renal clearances following diversion through 4½ in. ileal segment.

renal function during the course of these changes (Fig. 12). Whilst the blood urea curve shows a rise up to the third week after operation, followed by a fall to normal levels, the clearances are shown to increase steadily to a maximum value nine weeks after operation when they reach a figure almost twice those of the pre-operative period. The volumes cleared of creatinine, urea and P.A.H. increase in step with each other over the same time interval, whilst maintaining the relationship we would expect from their differing individual characteristics of renal excretion. This internal consistency affords perhaps the best evidence of the validity of these figures, which is supported by the marked simultaneous rise of maximum tubular excretion of P.A.H. being at nine weeks nearly three times its first post-operative level.

In another animal (Peggy, No. 33, 11 kg.) a similar series of estimations was made. In this dog, however, we first diverted all the urine through a

very short ileal loop (1½ ins.), and performed clearance tests. At operation, the short loop was replaced by a long one (7 ins.) and studies were made in the weeks after operation (Fig. 13). The familiar pattern of biochemical changes was seen, again with the highest level of blood urea occurring three weeks after the second operation. Clearance estimations again showed a rise, sustained beyond that time, and again reaching a peak for P.A.H. and urea at the ninth week. Creatinine clearance in this animal was consistently higher than before operation, though at a constant rather than a rising level. Tubular maximal excretion again rose steadily after operation, and at the eleventh week was nearly three times its first post-operative level.

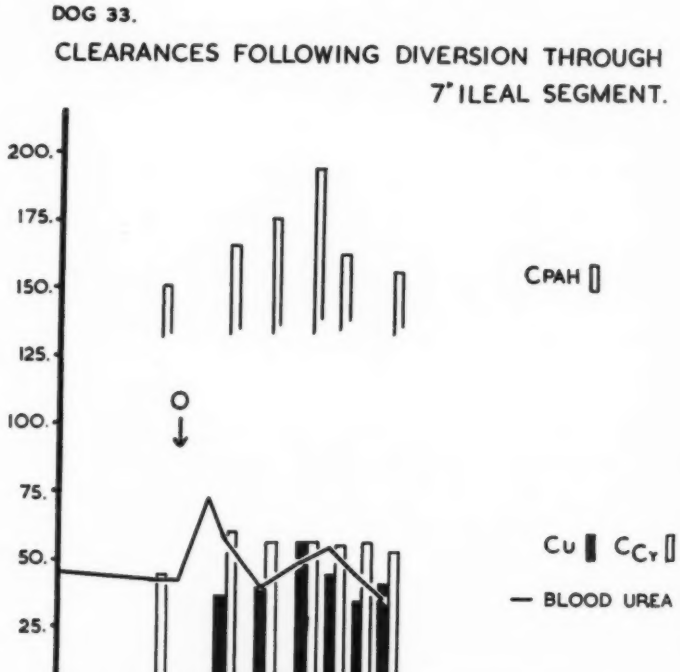


Fig. 13. Renal clearances following diversion through 7 in. ileal segment.

Although from the evidence of former experimental work it did seem inherently probable that there was a real increase in renal excretory capacity as a response to the reabsorption resulting from urinary diversion, I believe that these experiments represent the first occasion of its demonstration and measurement in terms of renal function tests. The conception is one that is, I find, difficult to appreciate against the background of our clinical experience that the sequel of transplantation is so often renal deterioration.

Because of the hesitation with which this change of outlook can be accepted, I was anxious to gather any possible evidence that might relate to it. It appeared that it would be helpful to measure renal function by some method that differed in technique at least, if not in principal, from the classical renal function tests. I have noted already that these depend upon accurate urine collection, and this can present special difficulty after diversion into the intestinal tract. I was at once attracted, therefore, by the study of renal function with radioactive iodine-labelled diodrast when I saw its use by Dr. Chester Winter in Los Angeles. In this method an estimation is made of the uptake and output of the radioactive substance as detected by a Geiger counter placed over the kidney. As it does not involve the collection of urine samples, it seemed particularly appropriate for the study of renal function after urinary diversion. I was most fortunate in being offered the use of some of the first radioactive diodrast available in this country.* In its use at the Buckston Browne Farm, Dr. John Fowler and the staff of his Department of Physics at King's College Hospital carried out the estimations of radio-activity, and interpreted these for me, for which I express my warm gratitude.

We first demonstrated that diodrast is not significantly reabsorbed from the ileal mucosa, a finding which enhances the value of the test in this field. We carried out tests on the two animals previously studied before and after operation with a Geiger counter over the left kidney. The count rate per minute is plotted as a curve that has been named the radioactive diodrast renogram (Fig. 14). It shows a sudden increase within a few seconds of injection of the radioactive material, with usually two peaks between one and three minutes in dogs. This is followed by a rapid decrease of counting rate at three to eight minutes, and a final phase which represents a slow elimination of the diodrast that has diffused through the plasma. It is the rapid decrease which is of main interest. The slope of this part of the curve is proportional to the clearance of diodrast by the kidney. It can be measured with some accuracy by plotting the curve on semilogarithmic paper, and subtracting the straight line found for the final slow phase from the full curve (Fig. 15). The

* For this I am indebted to Professor McMichael of the Postgraduate Medical School of London at Hammersmith Hospital, in whose medical unit clinical trials are being performed with material made first at the Radiochemical Centre, Amersham, and later in the Department of Physics, Hammersmith Hospital. I much appreciate their generous cooperation in making this material available to me.

slope may be described by a half period ($T \frac{1}{2}$) or equally well by an elimination rate of the amount of diodrast present in the kidney. Estimations on these two animals (Nos. 36 and 33) before and after the operation of diversion showed an increase in this rate of two and a half and three times respectively.

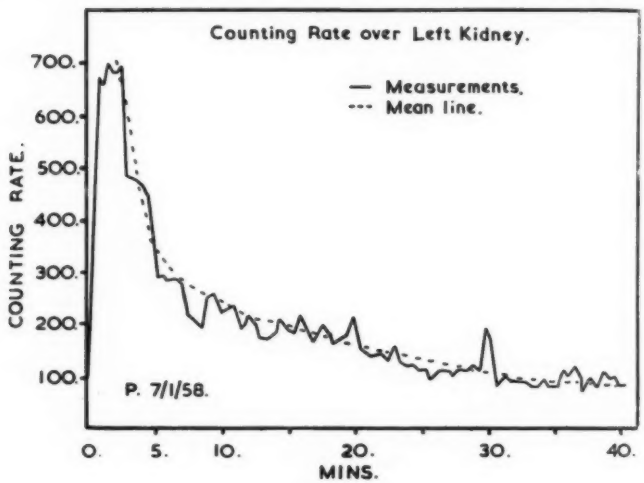


Fig. 14. Radioactive diodrast renogram.

I must stress that this method is still under development, and the samples of diodrast we have used have varied in specific activity. But I wished to note the value of this test in estimating kidney function after diversion, and I felt the correspondence of the findings with those of the classical clearance tests is of interest.

A review of the experimental work on diversion performed over the years recalls attention to the important effects of reabsorption of urinary constituents and the response of the kidney to the environmental change which thereby results. The general effects of weight loss, apparently from dehydration, and increased fluid intake and output are evidence of an effect upon the kidneys in the nature of an osmotic diuresis. The biochemical changes which have been noted are consistent with this interpretation. They have demonstrated that the disturbance resulting from reabsorption may be great enough to cause death in uraemia and acidosis, without hyperchloraemia or hypokalaemia. When the reabsorption is less, and compatible with survival, they show a pattern of changes in which blood levels are restored nearly to normal values. The view that this is a compensatory response on the part of the kidney to an increased excretory load is supported by the findings on post-mortem examination, in which

a marked renal hypertrophy has been demonstrated. It has been shown by observations submitted in this lecture that this hypertrophy reflects an increase in renal excretory capacity as measured by the classical clearance methods, and some confirmation of this finding is given by early studies with radioactive diodrast. At the same time there is histological evidence of a deleterious effect causing tubular damage, and it has been an experience under experimental conditions that when the kidneys have been strained to the limit of their adaptive capacity, sudden deterioration and death may occur.

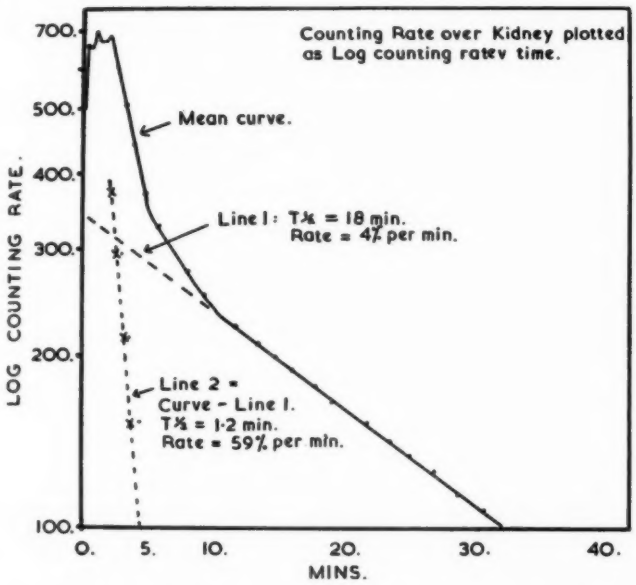


Fig. 15. Rate of elimination of diodrast from kidney, plotted from renogram.

We are continuing study with the ileal segment preparation to confirm and extend these observations; yet we have by now seen this pattern of changes with sufficient consistency to feel they were worth reporting for your interest. Their interpretation is of course open to discussion, but I would like to offer one conception of the conclusions they suggest. I believe that these findings help us to appreciate the nature and scale of the load imposed upon the kidneys when the urine is diverted across any wide area of absorptive mucosa, or equally to a limited area for a prolonged period. Our conception of these has perhaps been based too much upon the variations in blood levels consequent upon urinary diversion in clinical practice. Though such changes may point to the inherent dis-

turbance in a primarily renal failure, they are not so sure a guide to the defect of function involved when a previously normal kidney has its reserves overwhelmed by an excessive load, in what may be thought of as a secondary renal failure. Under these circumstances, those reserves, which have themselves been augmented to meet the new demand, are fully extended in maintaining blood levels at a normal value. Study of the point at which they break down may not by any means fully portray their achievement. Another circumstance that has, I believe, influenced our views on this problem is the fact that in clinical practice passage of the urine over a wide area of mucosa occurs only with diversion into the colon. The colonic mucosa is characterised by its avid absorption of chloride and hyperchloraemia is frequently observed. Patients running into imbalance after urinary diversion have been observed to have hyperchloraemia and acidosis, and they have responded well to measures that combat both of these. This has inclined us perhaps to overrate the importance of hyperchloraemia as a cause of the imbalance, or at least to give us an incomplete picture of it. A third factor that has, I feel, clouded understanding of these changes subsequent to diversion is the hard-won appreciation of the innocence of high-blood levels of urea itself in primary renal failure of pre-renal, renal or post-renal origin. This has possibly tended to a persuasion that urea has no deleterious effect, whereas in fact it may be a lethal agent (Hartman, 1933 ; Streicher, 1928). It is a paradox that in primary renal failure, high blood levels of urea may be tolerated without ill-effect, whereas lethal doses of this substance may not result in high blood levels, in animals with normal kidneys. The explanation of this may well be that the deleterious effect of urea is the result of its disturbance of osmotic equilibrium. Its effects are therefore likely to be dependent upon the rate of its passage through the kidney, rather than its concentration in the blood—more particularly when high blood concentration is the result of primary renal failure. Whenever the urine is liable to reabsorption there is the possibility of such a high rate of passage of urea through the kidney. The rapid absorption of urea from the intestine has been noted in the past, for example, by Annis and Alexander (1952), who were struck by the speed with which it was taken up from a segment of the colon. Yet no particular importance has been attached to the likely consequences. I believe that the past and present experimental studies that I have presented help to remind us of these, and indeed that through them the surgeon may see a clearer picture of the effects of diversion into the intestinal tract. I submit that when the area of mucosa is a wide one, or the time for which the urine is exposed to it is prolonged, the reabsorption of urinary constituents becomes of importance. First among these is urea, and the need for its elimination as it is recurrently presented to the kidney sets up an osmotic diuresis that may overwhelm the capacity of the kidney to maintain the internal environment. This obligatory diuresis particularly embarrasses the renal tubule in its task of retaining the acid-base equilibrium. When the mucosa involved is that of the colon, addi-

tional disturbances occur as a result of its peculiar properties of absorption and elimination. The most notable of these is that of chloride absorption, and if hyperchloraemia develops, it will aggravate the tendency to acidosis. I think this conception helps to explain the discrepancy that has been noticed between the incidence and degree of hyperchloraemia and of acidosis.

It is interesting to speculate whether the renal adaptive changes that I have described in the experimental animal also occur in man. There is little evidence about this. Though not the rule, we sometimes see in clinical practice a rise and subsequent fall in blood urea after an operation for urinary diversion. This would seem to be most readily explained as a renal response, yet the conception is not supported by the observations of Sauer (1949) on the few cases in which he undertook the exacting task of estimating renal function after uretero-colostomy. Nevertheless, it can be said at least that there is often a broad consistency in studies of comparative physiology, and the existence of a compensatory renal response in these circumstances would be compatible with the behaviour of the human kidney in disease, in which its capacity for adaptation is notable (Platt, 1952). If such a compensatory response occurs in man, it might help very much to explain our experience that young persons tolerate urinary diversion better than their seniors, for it would be tempting to link this with a greater capacity for renal response in the young.

"I could tell you of visions and dreams upon the subject."—WM. BLAKE.

A fundamental need is that of correct selection of patients in relation to their renal status. I believe that in the future we must learn to assess not only if the kidneys' function is normal or diminished, but also their capacity to respond to an increased load. In clinical practice, such a load is met chiefly after uretero-colostomy. It would be desirable to select for it only those with a renal capacity which would find the added burden well within their compass, for it is an experience of experimental and clinical work that when renal capacity is fully extended, there is imminent danger of a rapid and fatal imbalance. This operation entails some manipulation of the ureter, and the risks thereby imposed must be met by perfection of operative technique. In addition, the physiological problems are complicated by the unique properties of the colonic mucosa. First among these is that of the increased absorption of chloride, and on this Pyrah (1957) has recently shed an interesting light. He has demonstrated that, after diversion, the colon may undergo an adaptive change whereby chloride absorption is diminished. Hypokalaemia and hypocalcaemia pose their special problems of management. I have not seen the former in these ileal loop preparations, and regard it as arising, like hyperchloraemia, largely from the special activity of colonic mucosa, whereas calcium loss may be expected to be linked with acidosis. Yet it is my thesis that there is an underlying problem resulting from reabsorption that is a renal responsibility. If it can be met, the subsequent complications

may be minimised. One assistance we can render is to advise our patients not to diminish their fluid intake for the convenience of less frequent voidings, since the disturbance resulting from reabsorption is that of an obligatory osmotic diuresis that involves high fluid intake and output. I have mentioned only briefly the deleterious effects upon the kidney which have been observed. We do not know if they are caused by the same factors which stimulate hypertrophy, or by quite separate ones. I am sure it is a matter worthy of close attention. Equally should we seek any possible way of protecting the kidney from the one, and assisting it in its response to the other. I have long considered the possible value of the androgenic steroids in this role. MacKay (1940) described their renotropic effect of enhancing the hypertrophy of the remaining kidney after nephrectomy, and Selye (1939) that of protecting the tubules against damage in experimental hydronephrosis and corrosive sublimate poisoning. They would appear to fulfil some of our requirements in the field of uretero-intestinal anastomosis. I already have some indication of their effect in an experimental study, far too slight as yet to present for your critical consideration. Now that steroids of enhanced renotropic effect with minimal androgenic properties are becoming available, we are planning their investigation as being of possible value.

I hope you feel that in this field animal study has made some contribution to our understanding of the inherent problem. The sign of "Cave Canem" has stood before the door of surgery in this country in letters somewhat bold in relation to the danger of which they warned. This is the more surprising since John Hunter, an early master of that house, in whose memory this lecture is given, first taught us the value of comparative studies, now nearly two centuries ago. I am most grateful for the opportunity of working in the research farm of this College that has benefited so amply from his legacy.

FURTHER ACKNOWLEDGMENTS

I must express my gratitude to Professor Charles Gray and Dr. Mervyn Smith and the staff of the Department of Chemical Pathology at King's College Hospital, and also to Dr. Riley and staff of the Group Laboratory at Brighton, for their kind assistance with biochemical estimations and their interpretation. Professor D. Slome, Director of the Buckston Browne Research Farm, has throughout given his warm interest and assistance to this project.

REFERENCES

ANNIS, D., and ALEXANDER, M. K. (1952) *Lancet* **2**, 603.
ANDREWS, E. (1927) *Arch. Int. med.* **40**, 548.
ATCHLEY, D. W., and BENEDICT, E. M. (1927) *Proc. Soc. exp. Biol. Med.* **24**, 424.
BAIRD, J. S., SCOTT, R. L., and SPENCER, R. D. (1917) *Surg. Gynec. Obstet.* **24**, 482.
BELT, E., EBERT, C. E., and SURBER, A. C. Jnr. (1939) *J. Urol.* **41**, 482.
BISGARD, J. (1943) *Ann. Surg.* **117**, 106.
———— and KERR, H. (1948) *Arch. Surg.* **59**, 588.
BOLLMAN, J. L. and MANN, F. C. (1927) *Proc. Mayo Clin.* **2**, 134.
————————————(1927) *Proc. Soc. exp. Biol. Med.* **24**, 923.
————————————(1935) *Arch. Path.* **19**, 28.
BOYCE, W. H. (1951) *J. Urol.* **65**, 241.

BOYD, J. D. (1931) *Amer. J. Dis. Child.* **42**, 366.
BRICKER, E. M. (1950) *Surg. Clin. N. Amer.* **30**, 1511.
COFFEY, R. C. (1911) *J. Amer. med. Ass.* **56**, 397.
CORDONNIER, J. J. (1949) *Surg. Gynec. Obstet.* **88**, 441.
———— and SPJUT, H. J. (1957) *J. Urol.* **78**, 242.
CORTES, S. T. (1946) *Bol. Trab. Acad. Argent. Cir.* **30**, 558.
COUVELAIRE, R. (1951) *J. Urol. med. Chir.* **57**, 408.
DEPAGE, A., and MAYER, L. (1904) *Arch. klin. Chir.* **74**, 71.
FERRIS, O. D., and ODEL, H. M. (1950) *J. Amer. med. Ass.* **142**, 634.
FLINT, J. N. (1912) *John Hopkins Hosp. Bull.* **23**, 127.
GEER, W. A., and DRAGSTEDT, L. R. (1938) *Ann. Surg.* **108**, 263.
GERSUNY, R. (1898) *Wien. klin. Wschr.* **11**, 990, quoted by Foges.
*———— (1899) *Wien klin. Wschr.* **12**, 176.
GILCHRIST, R., MERRICKS, J., HAMLIN, H., and REIGER, I. (1950) *Surg. Gynec. Obstet.* **90**, 752.
GOODWIN, W. E., HARRIS, A. P., KAUFMAN, J. J., and BEAL, J. M. (1953) *Surg. Gynec. Obstet.* **97**, 295.
HARTMAN, F. W. (1933) *J. exp. Med.* **58**, 649.
HARVARD, B. M., and THOMPSON, G. J. (1951) *J. Urol.* **65**, 223.
HINMAN, F. A. (1923) *J. Urol.* **9**, 289.
———— and BELT, E. (1922) *J. Amer. med. Ass.* **79**, 1917.
———— and WEYRAUCH, H. (1936) *Trans. Amer. Ass. gen.-urin. Surg.* **29**, 15.
IRVINE, W. T., ALLAN, C., and WEBSTER, D. R. (1956) *Brit. J. Surg.* **43**, 650.
JOHNSON, T. H. (1956) *J. Urol.* **76**, 380.
KINGO, G. (1918) *J. exp. Med.* **27**, 449.
KINMAN, L. M., SAUER, D., HOUSTON, W. T., and MELICK, W. F. (1953) *A.M.A. Arch. Surg.* **66**, 531.
LAPIDES, J. (1951) *Surg. Gynec. Obstet.* **93**, 691.
LEADBETTER, W. F. (1951) *J. Urol.* **65**, 818.
LOWSLEY, O. S., and JOHNSON, T. H. (1955) *J. Urol.* **73**, 83.
MACKAY, E. M. (1940) *Proc. Soc. exper. Biol. and Med.* **45**, 216.
MARTIN, F. H. (1900) *Amer. Gynec. Obstet. J.* **16**, 395.
MAUCLAIRE, P. (1895) *P. Cong. franç. Chir.* **9**, 546-552.
————(1895) *Ann. Mal. Org. gén.-urin.* **13**, 1080.
MERSHEIMER, W., KOLARSICK, A., and KAMMANDEL, H. (1950) *Bull. N.Y. med. Coll.* **13**, 71.
NESBIT, R. M. (1949) *J. Urol.* **61**, 728.
NEWBURGH, L. H. (1919) *Arch. int. Med.* **24**, 359.
PARSONS, F. M., POWELL, F. J. N. and PYRAH, L. N. (1952) *Lancet* **2**, 599.
———— PYRAH, L. N., POWELL, F. J. N., REED, G. W., and SPEIRS, F. W. (1952) *Brit. J. Urol.* **24**, 317.
PLATT, R. (1952) *Brit. med. J.* **1**, 1313 and 1372.
POWELL, K. A. (1949) *Brit. J. Surg.* **36**, 421.
PYRAH, L. N. (1954) *Ann. Roy. Coll. Surg. Engl.* **14**, 169.
———— (1956) *Brit. med. J.* **1**, 135.
———— (1957) *J. Urol.* **78**, 683.
———— CARE, A. D., REED, G. W., and PARSONS, F. M. (1955) *Brit. J. Surg.* **42**, 357.
RUBIN, S. (1949) *J. Urol.* **60**, 874.
SAUER, H. R., BLICK, M. S., and BUCHWALD, K. W. (1949) *Surg. Gynec. Obstet.* **89**, 299.
SELYE, H. (1939) *J. Urol.* **42**, 637.
SIMON, J. (1852) *Lancet* **2**, 568.
SMITH, G. I. and HINMAN, F. Jnr. (1955) *J. Urol.* **74**, 354.
STAMEY, T. A. (1956) *Surg. Gynec. Obstet.* **103**, 736.
STEVENS, A. R. (1941) J. *Urol.* **46**, 57.
STILES, H. (1911) *Surg. Gynec. Obstet.* **13**, 127.
STREICHER, M. H. (1928) *Arch. int. Med.* **42**, 835.
TICHOFF, P. I. (1908) *Zbl. Chir.* **35**, 109.
TIZZONI, G., and FOGGI, A. (1888) *Zbl. Chir.* **15**, 921.
VERHOOGEN, J. (1908) *Assoc. franç. Urol.* **12**, 352.
VERMOOTEN, V. (1934) *J. Urol.* **32**, 273.
WELLS, C. A. (1956) *Brit. J. Urol.* **28**, 335.
WINTER, C. (1958) *J. Urol.* **76**, 107.
WITZEL, O. (1891) *Zbl. Chir.* **18**, 601.

* I am indebted to Dr. R. Oppenheimer of the Department of Urology, University of California Medical Center, for this reference to a case treated by Gersuny, with a discussion by Ewald and a reply by Gersuny himself.

POST-OPERATIVE STRICTURES OF THE BILE DUCTS

Lecture delivered at the Royal College of Surgeons of England
on
22nd April 1958
by
Rodney Maingot, F.R.C.S.
Surgeon, Royal Free Hospital, London

THIS LECTURE IS concerned solely with the man-made strictures of the bile ducts, which account for 80 per cent. of all the so-called benign or simple strictures of the bile ducts. No mention will be made here of the remaining 20 per cent. of benign or simple strictures, which include those due to external violence, congenital atresia, choledochus cyst, fibrosis of the duct caused by a long-impacted stone, stenosis of the sphincter of Oddi, sclerosing choledochitis, or recurrent pancreatitis.

Post-operative stricture of the bile duct is one of the most tragic complications seen to-day in the practice of abdominal surgery. Cattell (1958) rightly stresses that the occurrence of a bile duct stricture is a catastrophe not only to the patient but to the surgeon who performs the operation. The tragedy of this calamity can be gauged by remembering that 70 per cent. of the patients are women, 40 per cent. are under the age of fifty, and only about 60 per cent. of these cases are permanently cured by a reconstructive procedure. It is estimated that some 30 per cent. of such patients will eventually die from the attempts made to repair the stricture or from the effects of intermittent or complete biliary obstruction. Many of these unfortunate patients have had several unsuccessful operations for relief of the obstruction before being referred to a specialist in this field. I have had cases sent to me who were deeply jaundiced and cirrhotic and who had had as many as seven, eight or even nine previous operations for the correction of strictured ducts.

It is impossible to estimate the incidence of post-operative stricture of the bile passages, but there is no doubt that injuries of the common duct related to cholecystectomy have increased, and it cannot be questioned that the number of common duct injuries is much too great.

Cattell and Braasch (1958) have recorded a series of over 1,000 cases, and at the Mayo Clinic the yearly average number of such reconstructive operations amounts to about eighty.

No articles on this subject by British surgeons have appeared in the literature since 1944 (Walton, 1944; Grey Turner, 1944), apart from a number of personal contributions between the years of 1953 and 1957. This lecture is mainly based on the experience gained in performing eighty-one operations for bile duct strictures during the last twelve years.

Causes and prevention

The great majority of post-operative strictures follow cholecystectomy for chronic or acute calculous cholecystitis. Some follow in the wake of

exploration of the ducts for stone, partial gastrectomy for duodenal ulcer, excision of a diverticulum of the second part of the duodenum, or transduodenal sphincterotomy. The fact remains that about 80 per cent. of all benign or simple strictures of the bile ducts are the result of the surgeon's work, and that these grave complications of inept surgery are observed after the second most commonly performed abdominal operation in our hospitals to-day.

This unfavourable aspect of surgery of the gallbladder is sometimes used by physicians to justify conservative measures for the patient suffering from gallstones which cause minimal symptoms and for those who are seemingly asymptomatic. Statistics show that cholecystectomy for calculous cholecystitis, with or without exploration of the bile ducts, yields excellent results in about 85 per cent. of cases, and that the operative mortality is low, in uncomplicated cases rarely exceeding 1 per cent.

The operative death-rate in surgery of the biliary tract is related to the *delayed* treatment of gallstones and to the incidence of jaundice and/or choledocholithiasis. As more and more patients are subjected to cholecystectomy, an increasing number of common duct strictures are observed, not only in this country but also abroad, and notably in America. The tragedy is that they are largely avoidable.

Donaldson, Allen and Bartlett (1956), in analysing eighty-five post-operative strictures, have found that the injury to the common duct followed cholecystectomy in sixty-two cases, cholecystectomy combined with choledochostomy in nineteen cases, partial gastrectomy for duodenal ulcer in three, and portacaval shunt in one.

The real tragedy of stricture of the bile duct does not rest entirely on the extreme and protracted morbidity, the necessity for one or more repair operations in many cases, with appalling attendant economic loss and serious distress, or upon the immediate and delayed post-operative mortality ; the tragedy, as I have emphasised, is that they are, in most instances, avoidable.

It is more important to continue teaching the method of *prevention* of these strictures than it is to detail technical methods of reconstructing the bile duct. The seriousness of these surgical misdemeanours is so great that minute attention to the details of operative procedures on the biliary tract should be constantly stressed rather than minimised.

Success following cholecystectomy depends mainly upon referring patients with gallstones (and the complications of gallstones) to a surgeon who is experienced in this type of work, upon good assistance, good anaesthesia, excellent illumination, adequate incisions, a careful search for anomalies of the arteries and ducts, ligating and dividing the cystic artery *before* straightening out the cystic duct and demonstrating its junction with the main ducts, and exploring the bile passages in any case in which there is the slightest suspicion that there are stones in the biliary

passages. Drainage of the operative field should always be carried out as a routine measure (Figs. 1 and 2).

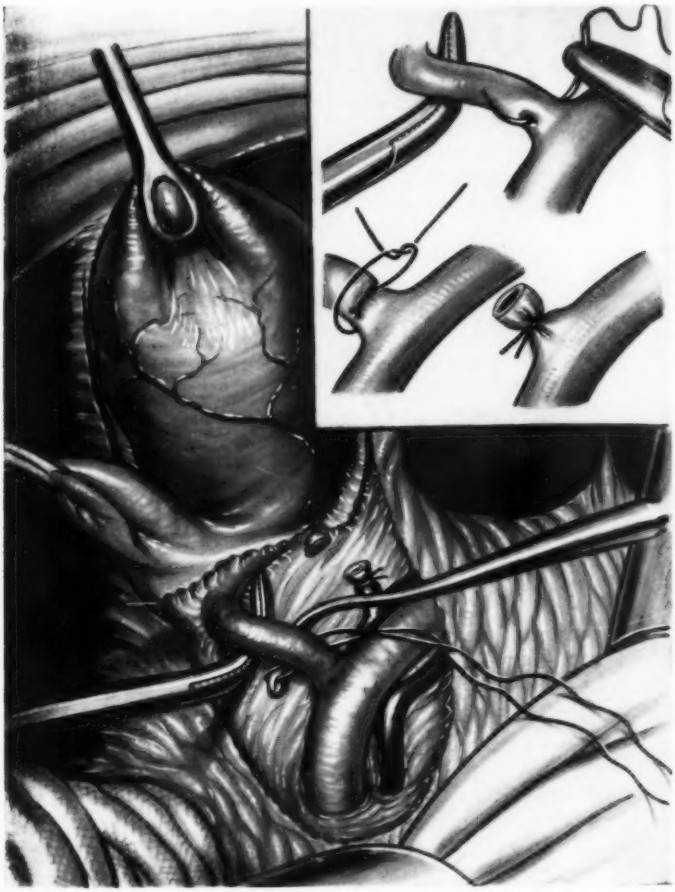


Fig. 1. Cholecystectomy, starting the dissection from the cystic duct end.

After the cystic artery has been identified, it is tied in continuity and divided. The convolutions of the cystic duct are then straightened out and the duct traced to its junction with the two main ducts. The cystic duct should not be clamped or ligated until this junction is clearly demonstrated.

Note that the cystic duct is ligated close to its junction with the main ducts. No stump is allowed to remain, as shown in the insert.

When the cystic duct is unduly capacious or fibrotic, it may be advisable to transfix and ligate the duct, as shown in the illustration.

For the sake of convenience, the causes of post-operative stricture of the bile ducts are best discussed under the following headings:

1. *Haemorrhage from the cystic artery, from an accessory cystic artery or from the right hepatic artery during excision of the gallbladder.* Bleeding from the cystic artery or from an accessory cystic artery can

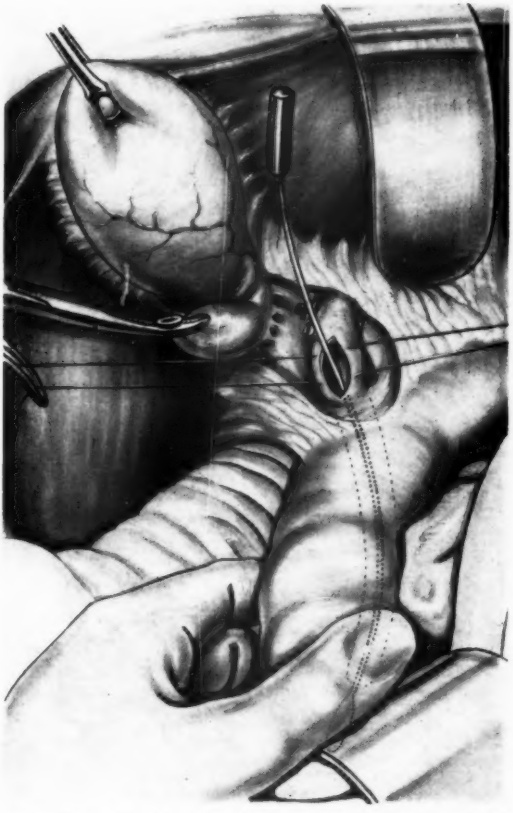


Fig. 2. Exploration of the bile ducts; cholecystectomy combined with choledochostomy.

The incision in the common duct is made through its anterior wall, just below the ligated stump of the cystic duct. After removing any stones which lie in this duct and thoroughly irrigating the whole ductal system with normal saline solution, graduated Bakes' dilators are passed into the duodenum to dilate the ampulla of Vater and the sphincter of Oddi. If no sounds can be passed into the duodenum, transduodenal sphincterotomy will have to be performed. These sounds must be passed gently and cautiously, otherwise considerable damage may be done to the lower reaches of the bile duct or false passages even be produced. Following the exploration of the bile passages, T-tube drainage is instituted.

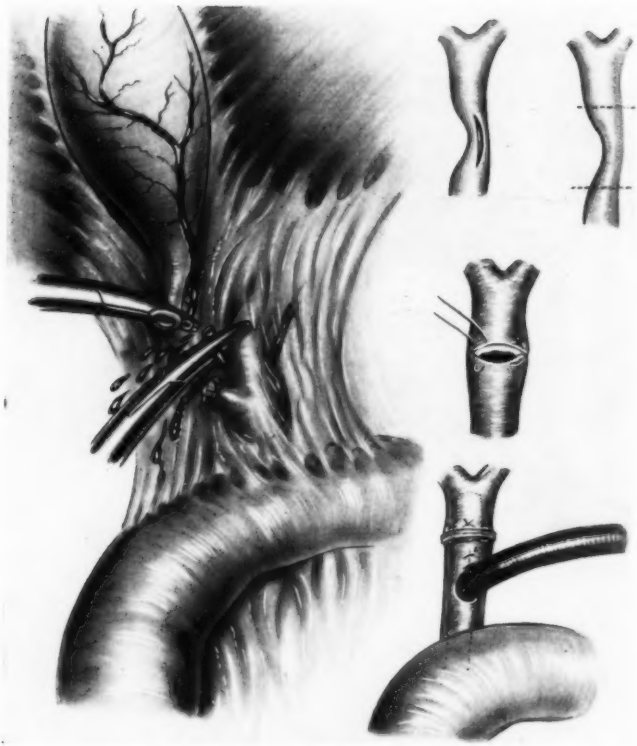


Fig. 3. Post-operative stricture of the bile duct.
Bleeding from the end of the cystic artery and the blind application of a haemostat which crushes a portion of the common hepatic duct. The partial stricture of the duct which results should not be repaired by the Heineke-Mikulicz procedure, as shown in the insert, but rather the strictured segment should be resected and an end-to-end anastomosis be carried out. Note that the T-tube is introduced into the duct below the reconstructed duct. The short arm of the T-tube acts as an efficient splint. All axial ductal unions should be splinted by the method shown, otherwise a quick recurrence of the stricture is to be anticipated. It is advisable to leave the T-tube *in situ* for a period of about six months.

be controlled by Pringle's method, which consists in inserting the index finger of the left hand into the foramen of Winslow and then compressing the structures in the free border of the gastrohepatic omentum, when the bleeding point can be visualised, picked up and ligated with relative speed and security.

It is possible to divide the right hepatic artery inadvertently when it runs parallel with and close to the neck of the gallbladder before giving

off its stumpy branch—the cystic artery; or, again, in retrograde cholecystectomy, the curving right hepatic artery may be rendered taut or acutely angulated, and if a haemostat is applied to the cystic duct in such cases, the lower end of the right hepatic artery will be tied to the cystic duct, while the top end will retract into the hidden recess behind the common hepatic duct and into the depths of the portal fissure. In this latter situation the haemorrhage is most difficult to control by any method, and the identification and secure ligation of the retracted upper end of the artery requires great skill.

As I have frequently stated, brisk bleeding from one of these arteries, a pool of blood, and a blind plunge with a haemostat for the spurting point, will frequently lead to a number of tragic events (Figs. 3 and 4).

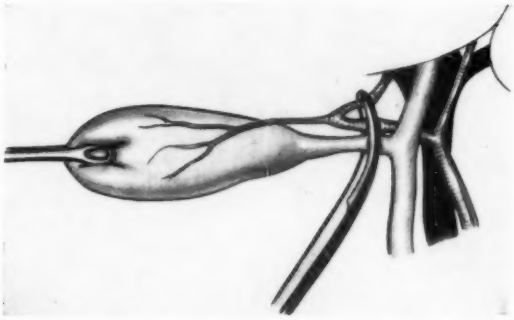


Fig. 4. A common cause of extrahepatic or hilar stricture of the hepatic duct. The single-clamp method.

As the surgeon pulls upon the liberated gallbladder, traction upon the cystic artery will so angulate the right hepatic artery that as the clamp is placed upon the cystic duct it will include the angulated right hepatic artery. This places the right hepatic artery under tension, so that as the ligature is placed about the cystic duct, there is a tendency, particularly for the upper end to retract out of the end of the ligature and result in serious haemorrhage in the hilus of the liver. Haemorrhage from the upper end of the right hepatic artery is the most common cause of injury to the common hepatic duct.

2. *The easy cholecystectomy*, during which too much traction on the gallbladder and cystic duct has led to tenting of the common ducts and to ligation and excision of a segment of these ducts. The easy case in a visceroptotic patient with a loosely attached gallbladder, the hurried operation, and the over-confident " showman " surgeon lacking in technical skill, all constitute a most sinister combination (Fig. 5).

3. *The difficult cholecystectomy*. Cholecystectomy is indeed a most difficult undertaking in cases where the gallbladder is small, shrunken, fibrotic and partly calcified, and lies high up close to the hilus of the liver. It often abuts against the common hepatic duct or the right hepatic duct, the planes of cleavage are difficult to identify, the arteries are distorted

and are encased in a sheaf of dense fibrous tissue, and in some instances there may even be a fistula between the gallbladder itself and the duct.

In such difficult cases it is advisable to open the common bile duct below the cystic duct, where it is readily accessible, and to insert a Liston sound into the right hepatic duct, this sound serving as a useful guide to the surgeon during his dissection.

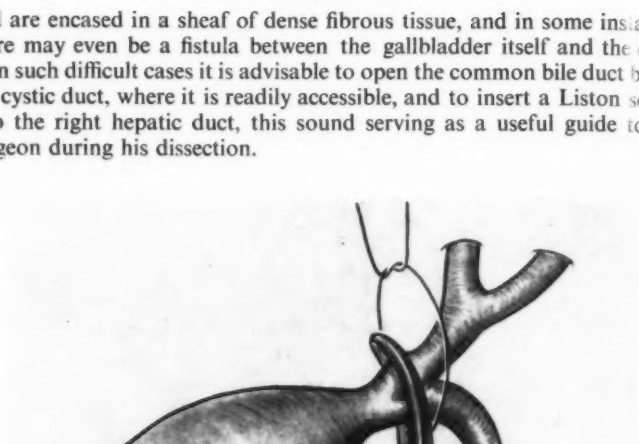


Fig. 5. Ligation of the common ducts during retrograde cholecystectomy (after Kehr.)
The method of reconstruction is clearly depicted.

Again, in some cases of acute cholecystitis the ducts may be unapproachable owing to the density of the adhesions and complete obscuration of the ducts and vessels by oedematous tissue. In such instances the wise surgeon will play for safety and perform cholecystostomy

rather than blindly excise the inflamed organ or carry out a partial cholecystectomy.

The surgeon has to be on his guard, too, where the cystic duct opens into the right hepatic duct; where it is unusually long, emptying its contents into the retroduodenal portion of the choledochus; and where no cystic duct is present, i.e., where the neck of the gallbladder opens directly into the main ducts.

4. *Suturing the cut edges of the right margin of the gastrohepatic omentum too tightly over the bile duct after cholecystectomy or choledochostomy.* It is inadvisable to suture this omentum over the small area occupied by the stump of the cystic duct and the cystic artery, as, should there be any post-operative bleeding or discharge of bile, these fluids will accumulate in the retroperitoneal tissues occupied by the bile duct. Should infection supervene in this space, the subsequent fibrosis may lead to stricture formation.

5. *Slipping of the ligature which has been applied to the cystic duct and/or the inadvertent division of an accessory hepatic duct.* In such instances a localised collection of blood and infected bile may pool and surround the ducts and in time cause a dense fibrous contraction of these passages. Bile is not only a cytolytic agent, but also a well-known sclerosant.

It seems probable to me that some of these cases of post-operative stricture of the bile passages are due to destruction of the bile ducts by the necrotising effect of bile that has collected in the peritoneal cavity and pooled in the region of the ducts. The necrotising and cytolytic effects of bile salts were demonstrated by Flexner and others many years ago, and have been amply confirmed. Dragstedt (1952) believes that damage to the ducts is often due to some agent, such as bile, acting from without, rather than to some process acting within the ductal system or to impairment of the blood supply.

6. *Mutilation or perforation of the common duct during the process of exploring it for stone or for fibrosis of the sphincter of Oddi.*

7. *During partial gastrectomy for a penetrating duodenal ulcer, the lower end of the common bile duct is in danger of being damaged by knife, clamp or suture.* About 3 per cent. of all bile duct strictures are observed after partial gastrectomy for the " difficult " duodenal ulcer.

8. *A lack of anatomical knowledge and of the appreciation of the anomalies of the bile ducts and cystic artery.*

The consequences of bile duct injuries

About 15 per cent. of injuries to the bile ducts are recognised during the conduct of operation. The correct treatment here is immediate reconstruction, preferably by an axial union between the ends of the duct, and T-tube splintage of the anastomosis—choledochostomy. The remaining 85 per cent. declare themselves post-operatively by: (1) profuse

and persistent discharge of bile through the abdominal incision ; should the external discharge cease, the ominous signs of jaundice and an epigastric swelling are quick to announce the gravity of the case and (2) deepening obstructive jaundice which, in the early phase of convalescence, is often attributed to retained common duct stone or to the evil effects of blood transfusions.

Some few patients who have sustained some operative injury to the ducts do not display the signs and symptoms of partial or complete blockage until some months or years after cholecystectomy. As fibrosis increases and the channel narrows, the signs of cholangitis and liver damage make a tardy appearance. Repeated intermittent attacks of fever, rigors and jaundice suggest a diagnosis of choledocholithiasis, and in fact such strictures are commonly associated with stone or biliary mud.

The effects of operative strictures of the bile ducts from an economic and social point of view are staggering. The icterus cannot be hidden and prevents normal social intercourse and daily work ; the intractable puritus causes insomnia ; rigors, pyrexia, anorexia and a stubborn type of malaise are constant findings ; liver damage is progressive and leads to biliary cirrhosis and portal hypertension ; and weight loss, due to recurring gastro-intestinal disorders, is marked. On top of all this, it is usual, as I have said, for the patient to have suffered the hopes and disappointments of more than one surgical attempt to restore the flow of bile into the intestines.

Preparation for surgery

All patients require an intensive course of pre-operative treatment. A high carbohydrate, high protein and low fat diet is given ; liver function tests are carried out on several occasions to determine the degree of hepatic damage present, as well as the response to the treatment prescribed ; prothrombin times are investigated in an effort to evaluate bleeding tendencies and vitamin K deficiencies ; the routine blood and renal function tests are undertaken to aid in ascertaining and computing the operative risks ; water and electrolyte imbalance is corrected by intravenous infusions of glucose and saline ; and blood transfusions by the slow-drip method, before, during and after operation, are given to correct anaemia and hypoprotinaemia. Massive blood transfusions should, however, be avoided. Antibiotic therapy is indicated when cholangitis or liver damage is present. It is customary to prescribe penicillin, 1,000,000 units, and streptomycin, $\frac{1}{2}$gm., daily.

A fistulous tract will demand adequate drainage, and if there is a profuse discharge of bile, continuous suction applied to an indwelling catheter will diminish the daily dressings and add to the comfort of the patient. In some cases a temporary ileostomy bag made of cellophane may be affixed to the sinus to reduce the number of dressings.

It has been my experience that those patients who are suffering from long-standing strictures of the bile ducts with associated portal cirrhosis

and hypertension do not require a splenorenal or portacaval shunt provided the obstruction can be completely overcome by a well-performed reconstruction operation.

Principles of repair

1. If the surgeon recognises that the bile duct has been injured during the course of an operation such as cholecystectomy, he should make every attempt at immediate repair (Figs. 6 and 7).

2. If it is at all possible to perform an axial or end-to-end anastomosis and thus preserve the sphincteric mechanism, i.e., by choledocho-choledochostomy or by hepaticocholedochostomy, this should be the procedure of choice (Fig. 8).

Fig. 6. Injury to the common bile duct ; immediate choledochocholedochostomy.

3. If an axial anastomosis is impracticable, the proximal end of the duct should be anastomosed to a loop of the proximal jejunum rather than to the duodenum. When a loop of proximal jejunum is employed, a long enteroanastomosis should be made in order to deflect gastric and intestinal contents away from the biliary-enteric stoma. Some surgeons

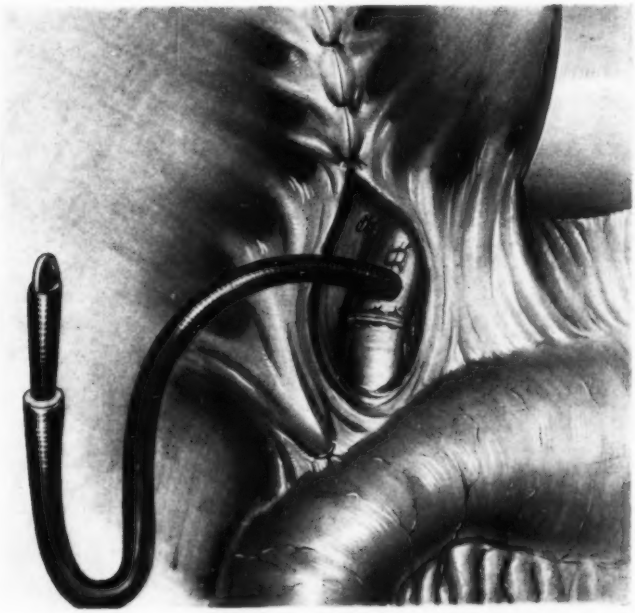


Fig. 7. Immediate choledochocholedochostomy.
The operation is completed.
In all such cases the subhepatic area is drained.

prefer the Roux-Y method, but in my opinion this more complicated type of anastomosis should be reserved for those cases in which the mesojejunum is unduly short (Figs. 9 and 10).

4. All anastomoses must be made accurately, without tension, and with interrupted sutures of Deknatel or fine silk. Mucosa should always be approximated to mucosa.

5. When an end-to-end ductal union is performed, the suture line should always be splinted by a T-tube. The long or vertical limb of the T-tube must not emerge through the suture line in the duct, but at a point above or below it.

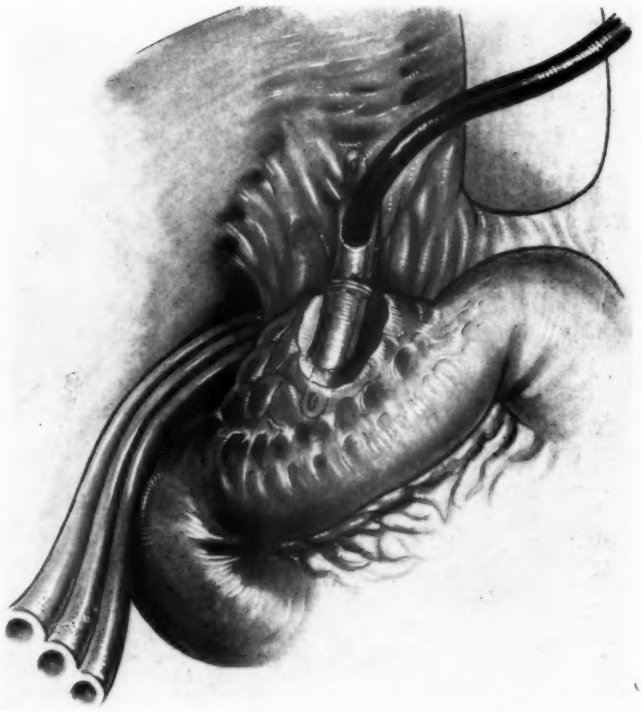


Fig. 8. Hepaticocholedochostomy; axial anastomosis, T-tube splintage and drainage.
Note that the lower end of the common bile duct has been dissected free from the sclerotic pancreatic head. Note also drainage of the subhepatic space with a corrugated rubber sheet.

6. Longmire's operation should not be considered unless an operative cholangiogram shows that the left and right hepatic ducts are in communication. This operation is rarely called for, and in most instances the results from its use are discouraging (Fig. 11).

7. In most cases it is advisable to display the portal vein and hepatic artery (and its branches) before dealing with the duct remnant, which may be extrahepatic or intrahepatic.

It should be noted that the *coring out of a biliary fistula* and the implantation of such a fistulous tract into the stomach, duodenum or jejunum is doomed to failure, although in a few published cases the immediate results appear to have been flattering. Bridging the gap or restoration of bile duct continuity with the aid of vitallium, polyethylene,

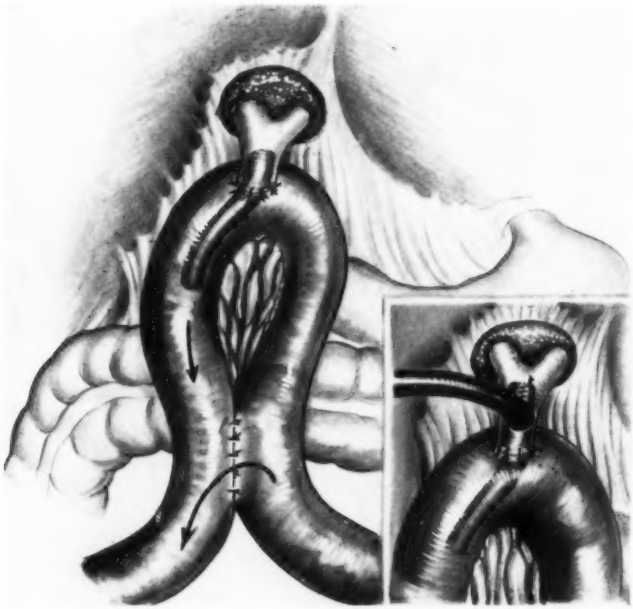


Fig. 9. Hepaticojejunostomy combined with enteroanastomosis.
Note the method of mucosa-to-mucosa anastomosis employing a single layer of interrupted sutures. Two methods of splintage of the stoma are illustrated. The method here depicted is one which has been most frequently employed by the writer.

rubber, silicone or other tubes is an interesting study in bile duct surgery. Unfortunately, however, all such tubes or prostheses sooner or later become blocked with cholesterol and calcium bilirubinate deposits and have to be withdrawn at a secondary operation. The ideal prosthesis, or an adequate heterogeneous or homologous substitute for an injured duct, has not yet been discovered.

Technique of repair of post-operative strictures of the bile ducts

The success of a common duct restoration depends upon the amount of proximal common duct available for anastomosis. Speaking generally, it may be said that, if the top end of the duct remnant is *outside the liver*, operation will be relatively easy, that some type of reconstruction can be carried out with safety, and that the prognosis will be good or excellent in fully 80 per cent. of the cases. If, on the other hand, the duct remnant lies deep in the liver, or at least *in the hilus of the liver*, the operation will prove extremely difficult. The anastomosis will be perilous, the

operative mortality high (approximately 10 per cent.) and the cure-rate low, possibly not exceeding 20 per cent. Again, over 50 per cent. of such cases will require one or more operations in an attempt to restore a satisfactory flow of bile into the bowel. My experience has shown that even after many failures, success may reward a determined and prolonged effort to correct this serious disability.

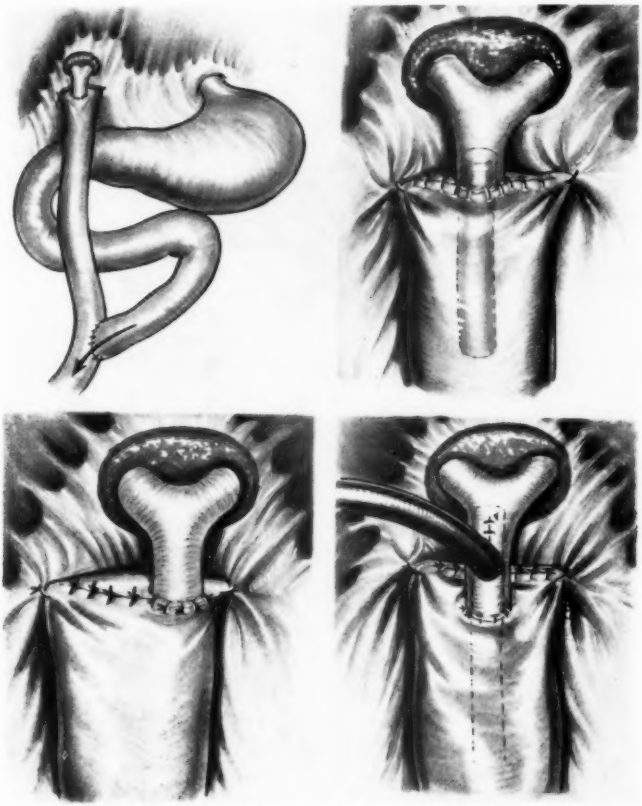


Fig. 10. Hepaticojejunostomy carried out after the Roux-Y plan.
Note the two methods of temporary splintage of the anastomosis with rubber tubes.

Here is a brief account of the exploration and essential steps of the operation :

A lengthy vertical incision, which extends well below the umbilicus (with the excision of one or more vertical laparotomy scars) ; freeing of

omental and visceral adhesions to the abdominal wall and liver ; mobilisation of the ascending colon and hepatic flexure ; packing the colon away from the field of operation ; the liberation of the stomach, the pylorus and the first part of the duodenum from the gallbladder fossa and the portal fissure ; the employment of Kocher's method of mobilisation of the second and third parts of the duodenum and of the head of the pancreas ; displaying the portal vein and the hepatic artery (and possibly its main branches) ; identification of the common duct gland which lies in an inferior position to the lower end of the duct ; and a scrupulous search for the bile duct or its attenuated remnants.

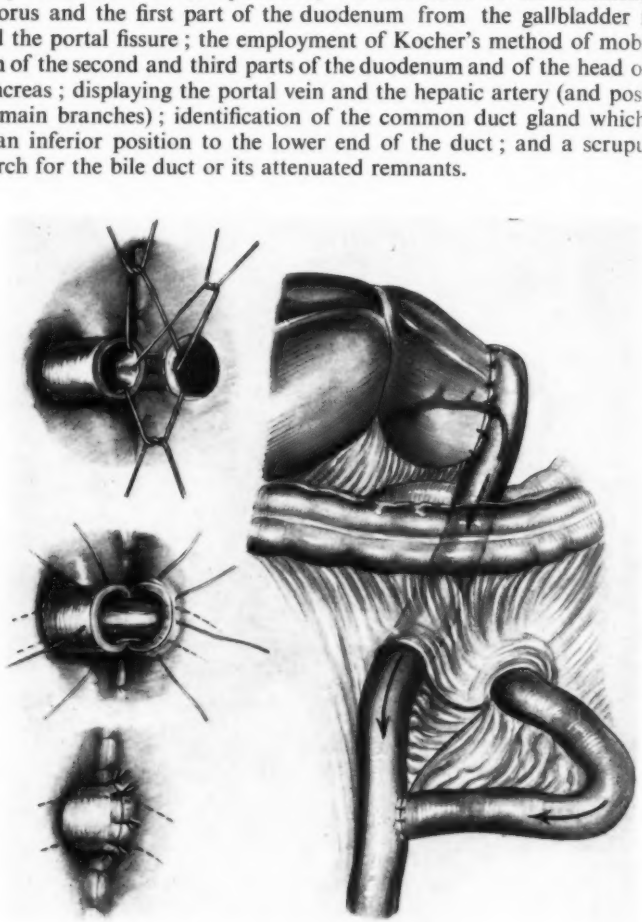


Fig. 11. Longmire's operation.

If there is a localised partial or complete stricture of the bile duct, it is better to excise all the scarred area and perform an end-to-end anastomosis followed by T-tube drainage and splintage of the suture line than to undertake the Heineke-Mikulicz type of repair or dilatation

of the stricture with graduated sounds. In three of my cases the Heineke-Mikulicz method was followed by a worse type of fibrotic stricture which called for subsequent resection of the strictured area and axial union of the healthy ends of the ducts.

If the upper and lower ends of the duct can be found and approximated without tension, end-to-end union should be carried out. Therefore, in those cases where the remnant of the hepatic duct is adequate in length, it is sometimes possible to anastomose this to the lower end of the common duct, which can be liberated from the head of the pancreas by knife dissection in an area just above the common duct gland or even by "splitting the head of the pancreas" to recover this portion of the duct.

If the mobilisation of the three portions of the duodenum and head of the pancreas has been thorough, it is a relatively easy matter to approximate the stunted lower end of the bile duct to the upper end of the hepatic duct in the portal fissure. There is no doubt that ascending cholangitis and other undesirable complications are unlikely to occur after ductal

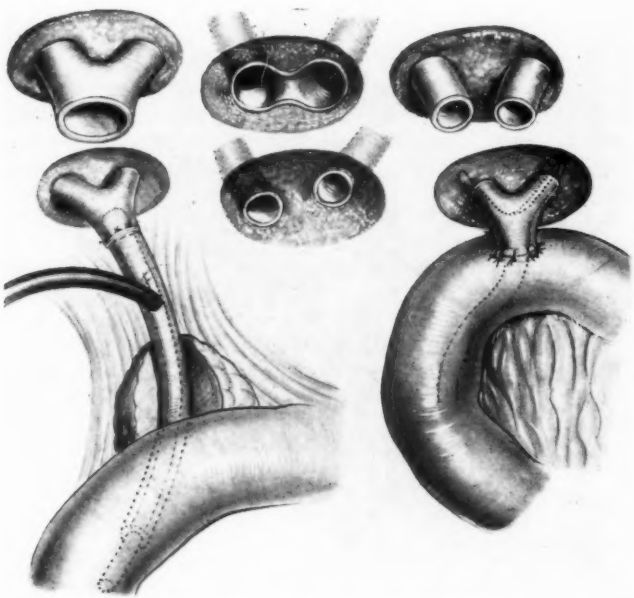


Fig. 12. Hepaticocholedochostomy; axial anastomosis and T-tube splintage and hepaticojejunostomy employing a Y-tube.
These Y-tubes are very rarely passed, and usually after a year they call for another operation for their removal through a small incision in the jejunum. The results following these two operations are generally highly satisfactory.

reconstruction if the sphincteric mechanism at the ampulla of Vater is preserved.

Most surgeons ignore the lower end of the duct, as it is commonly difficult to find, frequently atrophied and of smaller calibre than the recovered upper end of the duct ; moreover, the axial anastomosis, when completed, is frequently tight and strained.

In my own series of cases, hepaticojejunostomy, employing the jejunal loop method combined with a side-tracking anastomosis, was the procedure of choice. The majority of the cases in which the ducts were recovered in the portal fissure or deep in the liver itself were failures, and many were submitted to further operations to remove prostheses, such as Y-tubes, or to fashion further anastomoses.

Two patients with intrahepatic strictures, in which the ducts had to be displayed by coring out a substantial amount of liver substance with a diathermy loop, have remained symptom-free for four years or more. One of these patients had undergone eight previous attempts at reconstruction elsewhere without avail.

Hepaticoduodenostomy has proved an unreliable method in my hands, as partial or complete occlusion of the anastomosis has been a common sequel (Fig. 12).

Prognosis

The best results are obtained when the initial repair is carried out at the time of the injury or as soon after the injury as possible. With extrahepatic bile duct strictures, good results can be anticipated in some 80 per cent. of cases, but with hilar or intrahepatic strictures the cure-rate does not exceed 20 per cent.

The immediate mortality is about 10 per cent., and 30 per cent. of patients who have undergone bile duct reconstruction procedures die within a period of four years or so either from the operation itself or else from the effects of obstruction, i.e., from suppurative cholangitis, biliary cirrhosis, portal hypertension, hepatic coma, etc. Approximately 10 per cent. of all patients who live four years or more following operation have intermittent attacks of cholangitis, in other words, recurrent episodes of obstruction.

Because of the possibility of an eventual good result, each patient who develops recurrent signs and symptoms of bile duct stricture should be subjected to yet another attempt to repair it. If a patient is symptom-free after three years following bile duct reconstruction, the chances are that success has been achieved.

CONCLUSIONS

1. It is sad to reflect that about 70 per cent. of these unfortunate patients are women, that 40 per cent. are under the age of 50, that the immediate operative death-rate is about 10 per cent. and the late fatality-rate in the

region of 30 per cent., and that, all in all, less than 60 per cent. of these are eventually cured by reconstructive procedures.

2. The composite picture of common duct strictures is of such proportions as to demand increasing emphasis upon its prevention and the need for continued efforts to improve the results of surgical repair of these injuries.

3. The prognosis of extrahepatic duct strictures is good, while the outlook in cases of hilar or intrahepatic strictures, even when the operation is conducted by one experienced in biliary tract surgery, is very disappointing.

4. Success in the management of these cases depends upon many factors, such as the condition of the patient, the degree of liver damage, the presence or absence of portal hypertension, the amount of proximal duct which remains available for anastomosis, and the generalship of the surgeon together with his knowledge, experience and technical skill in dealing with such injuries.

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REFERENCES

CATTELL, R. B. and BRAASCH, J. W. (1958) *Lahey Clin. Bull.* **10**, 194.
———— (1947) *J. Amer. med. Ass.* **134**, 235.
———— (1958) Personal communication.
———— (1958) *Surg. Clin. N. Amer.* **38**, 645.
DONALDSON, G. A., ALLEN, H. W., and BARTLETT, M. K. (1956) *New Eng. J. Med.* **254**, 50.
DRAGSTEDT, L. (1952) *Surg. Gynec. Obstet.* **94**, 53.
GRAY, H. (1951) *Proc. Roy. Soc. Med.* **44**, 1005.
LAHEY, F. H., and PYRTEK, L. J. (1950) *Surg. Gynec. Obstet.* **91**, 25.
MAINGOT, R. (1953) *Ann. Roy. Coll. Surg. Engl.* **10**, 97.
————(1954) *British Surgical Progress* **1**, 1.
————(1955) *Abdominal Operations*, 3rd edition, p. 694. London, H. K. Lewis.
————(1956) *J. Irish med. Ass.* **39**, no. 230, p. 41.
————(1957) *The Management of Abdominal Operations* **2**, 851. London, H. K. Lewis.
TURNER, G. GREY (1944) *Lancet* **1**, 621.
WALTERS, W. (1953) *Ann. Surg.* 138, 609.
WALTON, J. (1944) *Surg. Gynec. Obstet.* **79**, 57.

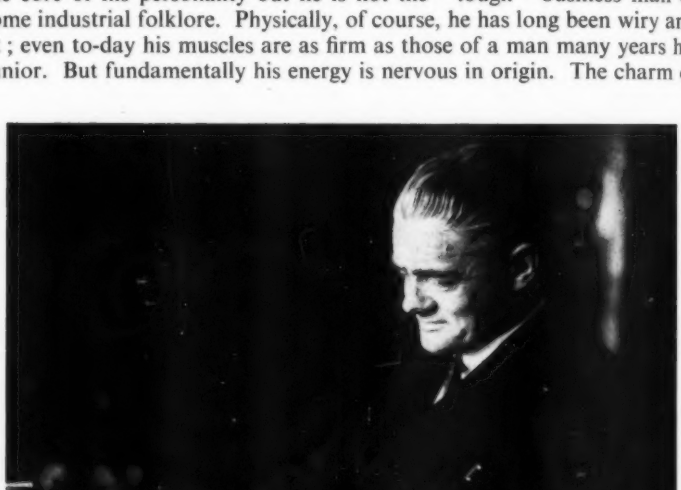
VISCOUNT NUFFIELD, G.B.E., C.H., F.R.S., Hon. F.R.C.S.

by

P. W. S. Andrews and Elizabeth Brunner
Members of Nuffield College, Oxford

WE, BELONGING TO Lord Nuffield's Foundation at Oxford, were pleased to be invited to write an article on him for the *Annals* of a more ancient Foundation, whose opportunities have been enlarged by the generosity and vision which brought our own College into being. Consideration of the mists which surround the legends of great benefactors of the past increases the feeling in both Foundations that we are lucky to be able to know and honour Lord Nuffield and the present authors have felt greatly privileged in being able to write a contemporary record of him and his work.

Lord Nuffield's career shows the drive and forcefulness which are at the core of his personality but he is not the " tough " business man of some industrial folklore. Physically, of course, he has long been wiry and fit ; even to-day his muscles are as firm as those of a man many years his junior. But fundamentally his energy is nervous in origin. The charm of



Lord Nuffield
(Published by kind permission of the Nuffield Organisation.)

manner which goes with his naturally imposing presence is the result of his awareness of other people. When he is with you, you feel that you are the one person to whom he wants to talk. If he has to make a speech he does not like to work it out beforehand but to speak as he is moved at the time ; then he holds his audience and carries its sympathy with him. This intuition of others is the key to his phenomenal ability at picking men to work with him and getting them to cooperate subsequently without any great administrative paraphernalia. This kind of reaching out of one's own personality is exhausting and the quietness and simplicity of Lord Nuffield's domestic life is a necessary counterbalance to his active business and public life. That our own biography said so little about Lady Nuffield was because she preferred to have only the bare minimum said. Here we can at least stress the importance of her contribution in the early days and since.

The traits of which we are writing explain that Lord Nuffield should be also sensitive to any feeling of unfriendliness. He does not find it easy to forget personal opposition. He did not accept the freedom of the City of Oxford, for instance, until 1951 when there was no member of the Council left who had had any connexion with the bitter, and, in one or two cases, interested, opposition to his introducing a bus service in 1913 to replace Oxford's long-obsolete horse-drawn trams. He likes straightforwardness and does not like being put off with " diplomacy."

He has managed his business on the same personal basis. His magnetic personality made people glad to work for him and made his local banker support him even, on one occasion, to the extent of enforcing the withdrawal of a negative decision by the main Board of the bank. In choosing managers he has looked for " loyalty " above all other qualities, and the ability to work with him. This meant they sometimes had to work by divination, because he expected his colleagues to know what was in his mind without having to spell it all out. They were given a free hand as long as they had his trust, but if they lost it they had to go.

His independent personality became clear early in life. William Richard Morris was born on October 10th 1877, of sturdy yeoman stock. He was a late developer and stayed at school till he was fifteen and a half, when his parents' ill-health forced him to become the breadwinner for a family of five. He was apprenticed in a bicycle shop, but being refused 1s. rise he started in business on his own. From a showroom in his mother's front parlour he prospered to a shop of his own, then bigger premises, workshops, motor cycle construction, garage and finally, as we all know, the manufacture of cars. It was not the unbroken progression such a summary might imply : he had two unfortunate experiences of partnerships which failed and from which he drew the lesson never to be dependent financially on anyone else ; but well before he was thirty-five he could have stopped with a successful garage and been content with a good income and a pleasant life had not a vision and purpose driven him on.

He spent some six years planning what sort of car he would make and turned all his experience as a garage mechanic to account to get a " complete car " with every part chosen for reliability and low maintenance costs and the whole at as low a price as possible. At this time, too, he adopted a principle which was as yet quite unrecognized in the British motor industry although it was of vital importance at the stage it had then reached : that it was the car manufacturer's role primarily to be an assembler and buy the parts from specialists who by their greater volume of production should be able to get much lower costs than any one small car manufacturer—and in those days all were small. Lord Nuffield's policy on buying-out only changed when the Morris orders became so big that they could absorb the entire output of independent suppliers.

Premises at Cowley were secured for assembly—where the Nuffield Organization still has its headquarters to-day. The first Morris Oxford was produced in 1913, but many had been sold in advance at the 1912 Motor Show on the basis merely of blueprints—with William Morris as his own representative. He was planning to add a second model, with the later famous name of the Morris Cowley, when the outbreak of war cut car production to a trickle. Munitions production showed him the benefits of really large-scale methods and the appropriate organization of supplies, but it was a severe check. With considerable courage, and in spite of a temporary breakdown of health in 1918-19 following on intense war work, he made a second start after the war.

Along with hundreds of other car manufacturers he was at first carried along in the post-war boom in the new motor industry. Some fifty new businesses appeared in a single year, and it is easy to see now that there were too many makes, and costs and prices were swept too high. In October 1920 came the crash in the markets and a slump which is remembered as more severe than anything the industry had later. Unsold cars cluttered up the floors and Morris's were faced with having to cease output, even though it is a maxim of Lord Nuffield's that a factory must be kept running full bore—" as long as the walls are bulging you cannot help but make profits." To the astonishment of both his staff and his competitors, Lord Nuffield took the decision to cut the price by £100. His demand picked up immediately and sensationally ; as production increased costs fell and justified the price cut, which was only the first of several. The price of the Morris Cowley four-seater just before the first price cut in February 1921 was £525 and by November 1921 its price was £341, and similar reductions, had been made in other models. Thereafter the Morris policy was settled : motoring for the million was here. The more recent history of the firm is common knowledge and need not be repeated.

Lord Nuffield's personal fortune grew almost incidentally with the success of his firm. It was the latter in which he was interested, but it was also a principle, after the experience of his early partnerships, that control

of his business should remain solely in his own hands. He therefore retained all the ordinary share capital of Morris Motors as long as he could himself, and the public were not admitted to ownership until 1936. Towards the end of the 1920s, however, the Inland Revenue brought two cases against him, to assess the undistributed profits of the Company to sur-tax. They failed each time, because it was held that the profits, which had been ploughed back consistently, were necessary for the development of the business, but it became clear to Lord Nuffield that he would have to change the structure of his business and of his life. Publicly-held ordinary shares required the more normal company-type of management set-up and a sharing of responsibility. From then on he withdrew more from management and began to plan the use of the wealth he was forced to realize personally. He has no children and he has devoted to his work as a benefactor the same care that he gave to building up his business.

Over his lifetime Lord Nuffield has given away some £28 million, and every gift has been pondered according to his vision of the kind of things that needed doing. In many fields he has sought out expert advisers who shared his vision but the interest he felt has decided where his money should go. His major benefactions fall under the broad headings of medicine, social research, and social welfare. Some of his earliest gifts (as indeed his latest) have been to medicine. When he was a boy it was his ambition to be a surgeon, but his family could not afford it ; nevertheless his business career has enabled him to be the greatest benefactor to medicine whom the British Commonwealth has known, and he may fairly claim to have done far more good than any one surgeon, however brilliant, could have achieved because of the resources which he brought to medicine when progress was so dependent on private benefactors.

True to character, where he has met a personality he could admire or trust he has backed his judgment financially. His first two large benefactions were because of personal contacts : in 1926 the foundation of the King Alfonso XIII Chair of Spanish Studies at the University of Oxford ; and a fund to enable parents to visit their children in Borstal institutions —this at the suggestion of that great humanitarian, the late Sir Alexander Paterson. The first big gifts to hospitals start in 1927, and were at first made primarily in the areas where the Morris factories were located, Birmingham, Coventry and Oxford. Later he got to know some of the doctors at Guy's Hospital who used to come down at weekends to Huntercombe Golf Club, and his gifts to Guy's range from magnificent buildings to the small, personal amounts given to reimburse nurses who had been the victims of a confidence trickster.

Lord Nuffield's interest in the Oxford hospitals grew into an interest in promoting research, and his first gift to the Nuffield Institute of Medical Research was followed by the creation in 1936 of the Medical School Trust. As will be known, Lord Nuffield this year intervened personally

to make sure that this benefaction should give priority to research. The whole development of the modern Oxford medical school has, however, been due to the lavish start given it by Lord Nuffield. Orthopaedic hospital work at Oxford has also been generously endowed so that the old Wingfield hospital has been transformed into the Nuffield Orthopaedic Centre, leading in both treatment and research. This reflects Lord Nuffield's keen interest in work for cripples which is also shown through the Nuffield Fund for Cripples, and the Nuffield Fund for Orthopaedic Services in Australia, New Zealand and the Union of South Africa. Another class of handicapped person for whom he has shown continuing concern is the blind. Apart from general donations to the national institutions for the blind, it was his money specially given which made possible the development of the talking books and the building up of a library in them.

His benefactions to the Royal College of Surgeons itself will be known to our readers. A grant of £250,000 in 1948 (since increased through his interest by benefactions from the Nuffield Foundation) created the Nuffield residential college which is to play such an important part in the training of young surgeons. Further grants since then have shown Lord Nuffield's personal interest in relatively neglected fields: the gift of £11,000 in 1951 to provide working funds for the Faculty of Anaesthetics at the Royal College of Surgeons reflects his interest in a department which was hardly recognized as an independent specialism until he himself insisted on a Chair in Anaesthetics as part of the medical school endowment at Oxford. In 1956 again he provided £100,000 for the Royal College to establish the Nuffield Research Chair of Dental Surgery.

We have not space to enumerate all his benefactions. Taking those over £10,000, some £8 million out of £25 million has gone to medicine. Of the remainder, other large trusts are his Benefaction for Employees, for his workpeople; the Nuffield Trust for the Special Areas, which helped to bring the areas employment from 1936 onwards; the Nuffield Trust for the Forces of the Crown, which did so much for the welfare of the services during the war, and still does; the foundation of Nuffield College for research in the social sciences; and finally his largest, most general trust, the Nuffield Foundation. This has as its objects the advancement of health, the advancement of social well-being, the care and comfort of the aged poor, the advancement of education, and other such charitable purposes as shall be declared by Lord Nuffield in his lifetime or after his death by all the Trustees. Lord Nuffield has chosen his trustees well, but long may he live to declare his own charitable purposes, as he has done so finely in the past.

ANATOMICAL MUSEUM

THE SPECIAL DISPLAY for the month of March consists of Hunterian specimens showing studies in development.

JOHN HUNTER'S STATUE

by

Jessie Dobson, B.A., M.Sc.

Curator of the Anatomy Museum, Royal College of Surgeons of England

ALMOST EXACTLY A hundred years ago, on 16th March 1859, the following letter was despatched to the persons mentioned therein :

"I am directed to inform you that at a meeting of the Council in Committee held on Saturday last, the 12th inst.

It was resolved :

That this committee feel that the reinterment of the remains of John Hunter in Westminster Abbey affords a most fitting opportunity to the members of the Medical Profession and others of raising a public memorial of their high appreciation of the Physiological and Surgical labours of John Hunter which have mainly tended to the advancement of the science of their Profession and to the high rank of British Surgery.

They therefore determine that a subscription shall be opened for the purpose of erecting a statue of

JOHN HUNTER

Resolved :

That the following gentlemen, in addition to the Members of the Council be invited to join this Committee :

The Trustees of the Hunterian Collection
The President and Censors of the Royal College of Physicians of London
The Master of the Society of Apothecaries of London
The Regius Professor of Physics of Cambridge
The Director General of the Army and Ordnance
The Director General of the Navy
} Medical Department
The President of the Royal Society
The President of the Linnean Society
The President of the Zoological Society
The President of the Geological Society
The Very Reverend the Dean of Westminster
W. H. Baillie, Esq.
Richard Owen, Esq.
Frank T. Buckland, Esq.

I have therefore to request that you will do the Council the honour of accepting their nomination and to inform you that the next meeting of the Committee will take place at this College on Tuesday the 29th inst. at 4 o'clock, at which they desire your attendance."

I have the honour to be,
Yours faithfully,
JOHN F. SOUTH, *Hon. Sec.*

John Flint South was elected President of the College in the following year. The appeal for subscriptions met with a most gratifying response for it seemed that public interest in the life and work of this great man had been reawakened after the publicity that his reinterment in Westminster Abbey had received and no less a sum than £1,213 0s. 6d. was collected during the next five years. The College contributed one hundred guineas and each member of the Council gave a separate donation. Other large amounts collected were fifty guineas from the Royal College of Surgeons in Ireland ; £50 from the Faculty of Physicians and Surgeons of Glasgow ; and sixty guineas from various medical societies in America through the good offices of Henry Ingersoll Bowditch (1808-1892), a pioneer specialist in diseases of the chest and Chairman of the first Massachusetts State Board of Health.

Henry Weekes (1807-1877), already notable as a portrait-sculptor, was commissioned to execute the work which was in effect a reproduction in marble of Joshua Reynolds' famous portrait. This was completed early in 1864 and on 11th March of that year at a meeting of the Council of the College a letter from Mr. Weekes was read in which he requested permission to exhibit his work in the forthcoming Royal Academy Exhibition. On 13th October it was reported to the Council and in the *Lancet* (ii. p.197) that the statue had been placed "in the south end of the Western Museum" ; and there it remained until a few years ago when that part of the museum became due for demolition.

Weekes's fee did not amount to the whole fund available and the residue was handed over to the College by the "Statue Committee" in 1867 "for award to the person to whom the Triennial Prize shall from time to time be adjudged."

PROCEEDINGS OF THE COUNCIL IN FEBRUARY

AT A MEETING of the Council on 12th February 1959, with Professor Sir James Paterson Ross, President, in the Chair, the following were admitted as Honorary Fellows of the College : Dame Lillian Penson of London ; Professor Adams A. McConnell of Dublin ; Dr. Richard Lewisohn of New York.

Mr. G. H. Macnab (Westminster) and Professor C. G. Rob (St. Mary's) were elected to the Court of Examiners for a period of three years from 12th March 1959. Mr. E. C. B. Butler (London) and Mr. S. H. Wass (Guy's) were re-elected for a period of three years from 8th December 1958.

The Council received with gratitude a gift from Mr. F. R. Moser, L.D.S. for the endowment of a Quintin Hogg Fellowship in Dental Research in the College.

The Hallett Prize was awarded to Dr. G. R. Duncan of the University of Otago, New Zealand, and also to Dr. H. L. Eaton of the University of Ceylon.

The Handcock Prize was awarded to J. C. Bull of Guy's Hospital Medical School.

Diplomas were granted as follows : Fellowship (1) ; Membership (132) ; Fellowship in Dental Surgery (19) ; Fellowship in the Faculty of Anaesthetists (37).

The following diplomas were granted, jointly with the Royal College of Physicians : Industrial Health (13) ; Medical Radiotherapy (1) ; Tropical Medicine and Hygiene (1).

The following hospitals were recognised under paragraph 23 of the Fellowship Regulations :

HOSPITALS	POSTS RECOGNISED		
	General (6 mnths. unless otherwise stated)	Casualty (all 6 mths.)	Unspecified (all 6 mths.)
CHELTENHAM — General Hospital (Additional)		Cas. Off.	
DARTFORD—West Hill Hospital (Additional)			*Under para.* 23 (*b*) S.H.O. (Ophth.)
LONDON—London Chest Hospital			2 Registrars or House Officers
ASHFORD, Middlesex — Ashford Hospital (Additional)	S.H.O.		Orth. Regr. Pre-reg. H.O. (Cas. & Orth.)
GRAVESEND — Gravesend and North Kent Hospital (Additional)	R.S.O. (from 1.8.58)	2nd Cas. Off. & Orth. H.S.	
ROTHERHAM—Moorgate General Hospital (Additional)	Pre-reg. H.S.		
ROTHERHAM—Rotherham Hospital (Additional)			Pre-reg. H.S. (Surg. and Cas.) Pre-reg. H.S. (Orth. and Cas.)
MEXBOROUGH—Montagu Hospital (Additional)	Pre-reg. H.S.		

Hospitals	Posts Recognised		
	General (6 mths. unless otherwise stated)	Casualty (all 6 mths.)	Unspecified (all 6 mths.)
Blackpool—Victoria Hospital (Additional)			S.H.O. (Thoracic)
London—Putney Hospital		*Confirmation of temporary recognition* 2 Cas. Offs.	
Birmingham—Selly Oak Hospital	*Extension of periods of recognition from 6 to 12 months* 2 Regrs.		*Under Para. 23(b)* *Periods of recognised training in the following Ophthalmological posts to be extended from 6 to 12 months.*
Birmingham—Birmingham and Midland Eye Hospital			Sen. Regr., S.H.O. and 2 J.H.O.'s
Chester—Royal Infirmary			Regr.
Maidstone—Kent County Ophthalmic and Aural Hospital			2 Senior Ophth. H.S.'s
Norwich—Norfolk and Norwich Hospital			Regr.
Southend—General Hospital			Regr.
Tunbridge Wells—Kent and Sussex Eye Hospital			S.H.O.
Wolverhampton—Wolverhampton and Midland Counties Eye Infirmary			Sen. Regr., S.H.O. and 2 H.O.'s
Reading — Royal Berkshire Hospital			Regr. and H.S.
Brighton—Sussex Eye Hospital			Regr.
Derby — Derbyshire Royal Infirmary			Regr. and S.H.O.
Portsmouth — Portsmouth and Southern Counties Eye Infirmary			Regr.
Southampton—Free Eye Hospital			Regr. and S.H.O.
Northampton—General Hospital			Regr. and S.H.O.
Pakistan — United Christian Hospital, Lahore			*Until February* 1962 2 H.O.'s
India—Sir Ganga Ram Hospital, New Delhi			2 H.O.'s

THE COLLEGE TIE

The design is a College crest (an eagle proper holding a mace of gold) repeated on a maroon background. The tie is made in pure silk or silk and rayon, and also available are squares in the same design and tubular scarves. These may be worn by the following: Fellows and Members of the College; Fellows and Licentiates in Dental Surgery; Fellows of the Faculty of Anaesthetists; holders of the special diplomas granted by the Royal Colleges through the Conjoint Board; postgraduate students attending educational courses at the College. The tie can be obtained from Messrs. T. M. Lewin & Sons Ltd., 1-3 Jermyn Street, St. James's, London, S.W.1.

APPOINTMENT OF FELLOWS AND MEMBERS TO CONSULTANT POSTS

R. COUNSELL, M.S., F.R.C.S.	Consultant Surgeon to Bermuda Medical Association of Hamilton, Bermuda.
J. O. ROBINSON, M.D., M.CHIR., F.R.C.S.	Consultant Surgeon to St. Bartholomew's Hospital, London, and to Gerrards Cross and Chalfonts Hospital.

The Editor is always glad to receive details of new appointments obtained by Fellows and Members, either through the Hospital Boards or direct.

DIARY FOR MARCH

Tues. 17	5.00	DR. M. O. SKELTON—Erasmus Wilson Demonstration—Some pathological lesions of the adrenal gland.*
Wed. 18		Board of Faculty of Anaesthetists.
	3.00	Annual General Meeting of Faculty of Anaesthetists.
	4.00	DR. C. LANGTON HEWER—Frederic Hewitt Lecture—Forty years on.*
Thur. 19		Pre-Medical Examination begins.
Fri. 20	5.00	Board of Faculty of Dental Surgery.
Mon. 23	5.00	PROF. A. SORSBY—Ophthalmology Lecture—Irregularly dominant affections of the retina.*
Fri. 27		Good Friday—College closed.
Sat. 28		College closed.
		Last day for applications for Annual Examinerships.
Mon. 30		Easter Monday—College closed.

DIARY FOR APRIL

Mon. 6		Surgical Lectures and Clinical Conferences begin.
Tues. 7		Final Membership Examination begins.
Wed. 8	5.00	SIR CLEMENT PRICE THOMAS—Tudor Edwards Lecture—Conservative and extensive resection for carcinoma of the lung.*
Thur. 9	2.00	Quarterly Council.
	5.00	PROF. T. J. S. PATTERSON—Hunterian Lecture—Congenital deformities of the hand.*
Fri. 10		Course in Clinical Surgery ends.
Tues. 14		Last day for nomination of candidates for the Council.
		Last day for nomination of candidates (F.D.S.) for the Board of Faculty of Dental Surgery.
	5.00	MR. G. L. BOURNE—Arris and Gale Lecture—The anatomy, physiology and pathology of the human amnion and chorionic membranes.*
Wed. 22		Second L.D.S. Examination begins.
Thur. 23		Association of Surgeons Annual Meeting.
Fri. 24		Association of Surgeons Annual Meeting.
		Surgical Lectures and Clinical Conferences end.
	4.30	PROF. J. H. LOUW—Moynihan Lecture—Observations on the pathogenesis and treatment of congenital intestinal atresia.*
Sat. 25		Association of Surgeons Annual Meeting.
Mon. 27		Dental Lectures and Clinical Conferences begin.
Tues. 28		Final Fellowship Examination (Ophthalmology and Otolaryngology) begins.
	3.45	MISS J. DOBSON—Arnott Demonstration—John Hunter's Museum.*
Wed. 29	5.00	MR. J. D. FERGUSSON—Institute of Urology Lecture—Cysts of the kidney.*
Thur. 30	5.30	PROF. M. A. RUSHTON—Otolaryngology Lecture—Cystic conditions of the upper jaw.*

* Not part of courses.

4

HYPOPHYSECTOMY IN THE TREATMENT OF BREAST CANCER

Hunterian Lecture delivered at the Royal College of Surgeons of England
on
17th April 1958
by

Andrew G. Jessiman, F.R.C.S.

From the Department of Surgery of Harvard Medical School at the Peter Bent Brigham Hospital, Boston, Massachusetts*

PHILOSOPHER, EXPERIMENTAL PHYSIOLOGIST, tireless investigator, Scotsman. Such was the man, John Hunter.

The process of growth was to attract his interest both in its normal form as an expression of ordered physiology and, as a clinician, when he encountered it as cancer in its uncontrolled form. Each of these four aspects of his personality must have been in part influential when he chose to study growth as he saw it in the antler of the deer. Since childhood he had observed this remarkable phenomenon. Here a bony structure sometimes five feet in length, carrying blood vessels, nerves and having an organized structure with a specific function was evolved within the space of ninety days. What were the factors that controlled this, initiating it and halting it at certain phases of the year? Surely this must be governed by some regulating mechanism as yet not clearly understood.

In order to pursue this interest he obtained permission to conduct experiments on the deer in Richmond Park. In July 1785 he had a buck caught and thrown and he ligated one external carotid artery. He knew that this vessel supplied the growing antler and the soft covering, the velvet, in which ran the nutrient vessels. On the following day, he noted that the half grown horn was cold and the pulsations of the velvet had ceased. He wondered whether it would be shed immediately or retained longer than usual. Two weeks later he was surprised to find that the pulsations had returned and growth continued. He had the deer killed and at autopsy found that his ligation of the external carotid had been correctly performed and deduced that the circulation to the antler had been taken up by a collateral anastomosis. This observation impressed Hunter and was to have far reaching effects on the course of vascular surgery. Although his main interests led him away from the studies of antlers, they were incorporated in the Hunterian collection and referred to by his brother-in-law, Sir Everard Home, who in his fourth lecture on comparative anatomy at the Royal College of Surgeons in 1810 wrote :

" When the testicles begin to enlarge in the beginning of May, the horns begin to bud ; when they are at their full vigour, the horns are completely formed and afterwards receive no further supplies ; so that they are no longer any

*This work was carried out under a grant from the American Cancer Society (Massachusetts Division), Inc. and a grant from the United States Public Health Service (C 2965). The assistance of The Upjohn Company and of Winthrop Laboratories, Inc., is gratefully acknowledged.

expense to the animal till they are thrown off. But if the testicles are removed after the horns have begun to grow, those horns are mewed, and replaced by others, which differ from the former in being smaller, and never arriving at perfection. They always continue soft, and covered with velvet; so that they retain their supply of blood and therefore continue alive; which explains their never being thrown off, a process that can only take place in consequence of the part having previously been deprived of vitality." (Home, 1810.)

Here were observations of great importance, first that antler growth was related to testicular activity and secondly that after castration, there persisted a further influence, now known to be a pituitary factor, which maintained growth. It was also seen that *with* this disturbance of hormonal mechanism, the growth that occurred was not normal.

It was a second Scotsman, also a surgeon and naturalist who in his study of the disordered growth of cancer drew attention once again to the antler and pointed out its relationship to the gonads. In 1896, Sir George Beatson in his famous treatise, "On the treatment of inoperable cases of carcinoma of the mamma," wrote:

"Thus in stags the yearly growth of the horns, which is local cell proliferation, is under testicular influence, for if a deer is castrated, its horns do not grow and, what is more remarkable still, if only one testicle is taken away, it is only the horn on that side that does not grow."

The inaccuracy of the latter half of his statement was overshadowed by the importance of his appreciation that both the ordered growth of the antler and the disordered growth of cancer were controlled by the sex glands. With the recent rapid development of knowledge in the field of endocrinology, it has been confirmed that many hormones besides the sex hormones are involved. In experiments carried out at Harvard University, Drs. Joseph Aub, Thomas Hall and Francis Ganong (Hall, 1958) have shown the importance of the pituitary factor in influencing antler growth. They carried out an hypophysectomy in a deer and, whilst supporting it with cortisone, testosterone and thyroid replacement therapy, observed that antler growth was minimal.

It is my privilege to present the results of a study which is the logical sequel of these inquiries into the nature of normal and abnormal growth —the treatment of advanced mammary cancer by hypophysectomy. This is the work of many in the Departments of Surgery, Medicine and Gynaecology at Harvard University Medical School and the Peter Bent Brigham Hospital. It is a signal honour for me that it has fallen to my lot to make this report.

THE RATIONALE

The clinical results obtained in the treatment of mammary cancer by hypophysectomy have established this as a valuable therapeutic tool. Before discussing it, the reasons behind its use should be examined.

Mammary cancer may be stimulated by:

Ovarian factors. The experimental and clinical importance of oestrogens in their direct action is well documented and will not be discussed

However, there is evidence of the presence of a further action mediated through the pituitary gland. Furth (1957) has shown that prolonged high oestrogen levels in mice will lead to pituitary tumours capable of secreting lactogenic hormone. Smith (1944) produced evidence that biologically inactive metabolites of oestrogens could stimulate the pituitary. Working with rats and using an oxidative inactivation product of oestrone, it was shown that this compound caused, in much smaller doses, a greater release of luteinizing hormone and adrenotropic factors of the anterior pituitary as did oestrone itself. Studies of human pituitaries in women developing mammary cancer may show that similar mechanisms exist in which ovarian activity acts as a trigger mechanism leading to the production of those pituitary factors which stimulate the disease.

Pituitary factors. Clinical evidence of the presence of such a factor was reported by Pearson *et al.* (1955). In a group of patients in a state of relapse following a remission obtained by previous adrenalectomy and oophorectomy, he obtained further remission with hypophysectomy. In these patients it might be assumed that oestrogenic activity was minimal and that the remission followed the removal of some pituitary hormone.

Growth hormone and lactogenic hormone. There has been much discussion as to the relative importance of these two hormones in mammary cancer. The synergistic action of these hormones and ovarian hormones on normal mammary physiology has been exhaustively studied (Lyons, *et al.*, 1955) and it is probable that a similar synergism exists in mammary cancer. Probably both hormones are important but it is our belief that growth hormone plays a dominant role. Positive evidence in support of the relative importance of growth hormone may be found in :

1. *Animal work.* In the rat it has been shown that it is growth hormone which is the main factor producing the proliferative changes in the lobulo-alveolar system seen in pregnancy. The action of lactogenic hormone is more clearly seen in lactation. Here the process is one of repair following the apocrine shedding of the surface of the cell. Inference *only* can be drawn by comparison between animal and normal physiology on the one hand and human cancer on the other but it would appear that it is the proliferative changes seen in pregnancy, mainly influenced by growth hormone, rather than the maturation changes seen in lactation which most closely mimic those seen in cancer.

2. *Clinical work.* Pearson reports evidence of direct stimulation of mammary cancer by human growth hormone. By giving human growth hormone to a patient in a state of remission following hypophysectomy, he was able to show a temporary exacerbation of the disease as measured by urine calcium excretion studies. (Pearson, *et al.*, 1957).

Indirect evidence as to the relative lack of importance of lactogenic hormone is seen in the results of pituitary stalk section. Animal work has shown that lactogenic hormone secreting cells persist following stalk section whilst the gonadotropic hormone secreting cells degenerate (Everett, 1958). One may assume that they persist also in the human following stalk section. Clinical results of this procedure have shown that a remission of mammary cancer may occur simultaneously with full

lactation in the remaining breast (Ehni and Eckles, 1958). This phenomenon of full functional activity occurring *pari passu* with cancer regression can be explained. Lactation in these patients occurs due to the persistence of lactogenic hormone, the presence of administered cortisone and the absence of oestrogen and progesterone. Regression of the cancer follows the removal of growth hormone and oestrogens.

In the light of our present knowledge such direct and indirect evidence of the importance of pituitary factors must act as a guidepost indicating hypophysectomy as a rational step in the endocrine treatment of breast cancer.

THE PROBLEM

The differing patterns of response to hypophysectomy pose a problem well illustrated by the following two cases :

Case 1. Mrs. H. F. (PBBH unit 2H153) was forty years of age when in June of 1953 she noticed a lump in the left breast. A left radical mastectomy was carried out for a Stage II carcinoma of the breast and was followed by a post-operative course of X-ray therapy to the axilla. In August 1953 a total hysterectomy and bilateral salpingo-oophorectomy was performed. In the post-operative period, she experienced hot flushes which were treated by the administration of stilboestrol 5 milligrams per day. This therapy was continued for three years until her first admission to the Peter Bent Brigham Hospital. In August 1954 a recurrence was noted in the left supraclavicular triangle. This was treated with X-ray therapy and regressed. She remained well until August 1955 when a similar recurrence was noted in the right supraclavicular area. This also responded to X-ray therapy. In February 1956 a recurrence was noted in the left radical mastectomy wound but was never completely controlled with X-ray therapy and she was admitted to the Peter Bent Brigham Hospital for the first time on 15th June 1956, for assessment as to future therapeutic measures.

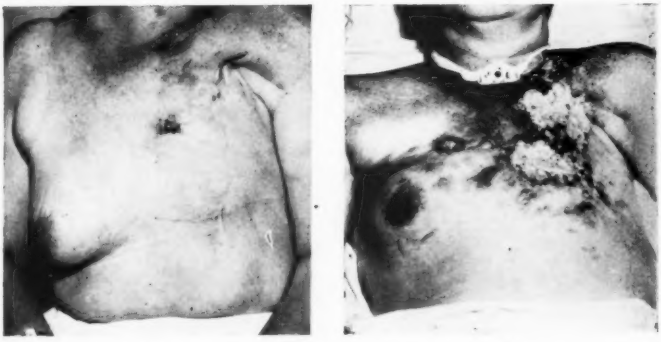
On admission, her general condition was good. She had scattered areas of cutaneous recurrence in the left mastectomy wound. These were not ulcerated. She also had an area of induration in the left infraclavicular and supraclavicular areas which were felt to be the result of her extensive X-ray therapy. She had palpable malignant glands in the right supraclavicular area. Examination of the abdomen showed no hepatic enlargement and there were no masses palpable. Investigations at this time revealed that there were no pulmonary metastases nor skeletal metastases. Urinary FSH determinations were negative from 50 to 200 m.u. per twenty-four hours and the urine oestrogen excretion was T_0 7,500 i.u.*. These latter determinations were felt to be a reflection of the oestrogen therapy over the previous three years.

Oestrogen therapy was terminated, but by one month later, it was apparent that the cutaneous metastases were spreading and she was placed on cortisone therapy (75 milligrams per day). By 3rd August 1956 it was obvious that the disease was progressing and she was readmitted to hospital. At this admission, it was found that the disease had extended into the neck and was causing respiratory embarrassment as a result of tracheal obstruction. To alleviate this, a tracheotomy was carried out on 7th August 1956. At this time, it was the concensus of opinion that the disease was progressing rapidly and that an hypophysectomy should be carried out at the earliest possible time. Pre-operative investigations showed the urinary FSH negative to 10 m.u. and the

*The normal postcastration urinary excretion levels are FSH positive to 200m.u. dilution and urine oestrogen T_0 less than 50 international units. Reference to levels will be made later in the paper.

urinary oestrogens T_{zn} less than 10 i.u. Urine calcium determinations ranged between 150 and 300 milligrams per day with the patient on a diet with a maximum intake of 200 milligrams per day. On such a diet, the normal urinary excretion of calcium is less than 150 milligrams per day. Vaginal smear determinations showed the presence of a cornified smear. I_{131} uptake was 22 per cent. per twenty-four hours and PBI 4.4 micrograms per cent. These are normal values. It was felt that the low FSH and the oestrogenic smear indicated the persistence of the oestrogen effects of the therapy she had discontinued six weeks before.

Hypophysectomy was carried out on 15th August 1956. This was uneventful, the gland being removed in one piece. Studies in the postoperative period indicated that hypophysectomy had been complete. The FSH was negative to 10 m.u., the I_{131} uptake 0 per cent. per twenty-four hours and the PBI fell to 0.6 micrograms per cent. Her post-operative course was steadily downhill. The cutaneous metastases on the left chest wall ulcerated and she was left with a fungating mass of malignant tissue covering the left infraclavicular area and extending up into the left neck. She died on 28th September 1956, six weeks after hypophysectomy. Autopsy was obtained and the pituitary gland was found to be absent and the sella turcica empty. There was no accessory ovarian tissue (Fig. 1).



(*a*) 3rd August 1956 (*b*) 20th September 1956

Fig. 1. Patient H. F. Anterior chest wall before hypophysectomy (*a*) and six weeks post-hypophysectomy (*b*). Progression of the disease was unchanged by hypophysectomy.

Case II. Mrs. E. H. (PBBH Unit # 5L909) was forty-five years of age when in November 1955 she underwent a hysterectomy and bilateral salpingo-oophorectomy for uterine fibroids. In January 1956 she noticed a lump in the left breast and one month later, underwent left radical mastectomy. This revealed carcinoma simplex and fourteen out of fourteen lymph nodes examined were involved with tumour. She received post-operative X-ray therapy to the axilla. In August 1956, right simple mastectomy was carried out, the histology showing adenofibrosis. She remained well until July 1957, when a mass was noted in the left supraclavicular fossa and chest X-ray revealed multiple pulmonary metastases. She was placed on stilboestrol 15 milligrams per day. Further X-ray examination in December 1957 showed an alarming increase in the number and size of the pulmonary metastases and she was referred to the Peter Bent Brigham Hospital for evaluation as to future therapy.

On admission, on 30th December 1957, her general condition was found to be excellent. Her only complaints were of lethargy and occasional coughing attacks. Physical examination showed one small hard gland in the left supraclavicular area. There were numerous adventitious sounds throughout both lung fields. Examination of the abdomen revealed no enlargement of the liver and pelvic examination was negative. Investigations showed a urinary FSH level negative from 20 to 200 m.u., urinary oestrogen levels T_o 10,000 i.u. and T_{zn} 37,500 i.u. These high levels of oestrogens are a measurement of the stilboestrol she had been receiving. This oestrogenic stimulation was further shown by the vaginal smear examination which showed a smear containing 92 per cent. cornified cells. Urine calcium excretion was 20 to 45 milligrams per day. Pulmonary function studies showed a moderate reduction in all values. It was felt that this patient's disease was advancing rapidly and that hypophysectomy should be carried out. Pre-operative thyroid function studies showed I_{131} 19 per cent. uptake per twenty-four hours and PBI 10.6 micrograms per cent.

Hypophysectomy was carried out on 4th January 1958. The gland was removed intact. Apart from a severe diabetes insipidus (29,000 cc. of urine being excreted in the first twenty-four hours) which subsided by the end of the first seven days, she had an entirely uneventful convalescence. She was discharged from hospital on the eleventh post-operative day. Post-operative investigations showed urinary FSH negative 2.5 m.u., urine oestrogens T_o 50 i.u., T_{zn} 250 i.u. Vaginal cytology showed a shift towards an atrophic smear. Thyroid functions studied showed I_{131} 7 per cent. per twenty-four hours uptake, PBI 0.8 micrograms per cent. By the date of her discharge, ten days post-operatively, X-ray of her chest already showed an improvement in her pulmonary metastases which were less apparent and smaller in size. She has continued to make good progress. (Fig. 2).

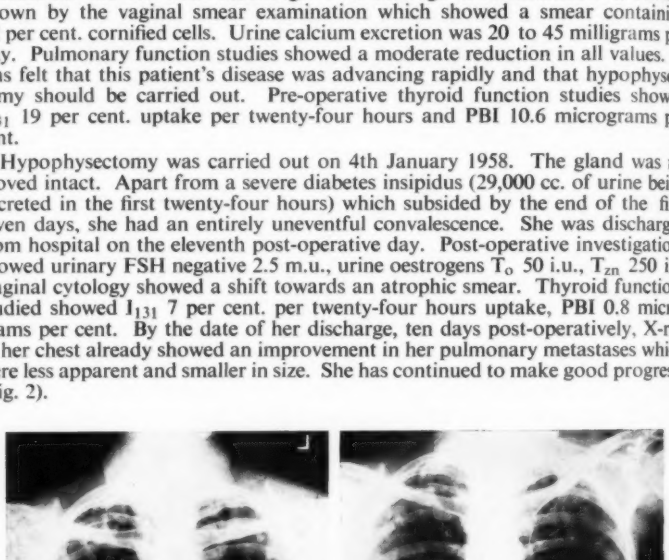


Fig. 2. Patient E. H. X-ray chest before hypophysectomy (*a*) and three months after hypophysectomy (*b*) showing decrease in size of pulmonary metastases.

Both of these patients were the same age, had undergone hysterectomy and oophorectomy and subsequently been treated with oestrogen therapy. Both had soft tissue disease, the first chest wall recurrence, the second

pulmonary metastases. Both were treated by withdrawal of the oestrogen therapy and by hypophysectomy.

Yet the subsequent courses of these two women were entirely dissimilar. In the first patient, the progress of the disease was unaffected and she went rapidly downhill to death. The second patient showed a prompt response with the clearing of her pulmonary metastases and an improvement which has been maintained and is increasing to the present time. The question must be asked as to what is the underlying difference in these two patients? It is in the hope that some truths may be uncovered which may help in the solution of this problem that the study of our patients has been carried out.

THE MATERIAL AND SCOPE OF THE STUDY

The statistical survey of the clinical efficacy of hypophysectomy and the comparative merit of hypophysectomy to adrenalectomy, with or without ovariectomy, has been left to others who have already embarked on such studies (Ray and Pearson, 1958 ; Atkins, 1958). Indeed, our Hospital with its small bed space, is not suitable for such a study. However, the closely integrated departments of Medicine, Surgery and Gynaecology and the readily available services of the School of Medicine at Harvard University make this Hospital particularly well adapted to an intensive study of the individual patient treated in this way.

All have been in the late stages of metastatic mammary cancer. All have been treated with previous oophorectomy and many have had prolonged courses of X-ray therapy and various forms of hormonal therapy. Since hypophysectomy was offered to any patient in the terminal stages of the disease, there was no selection of the patients undergoing the procedure. Once, however, the decision to perform hypophysectomy had been made, every effort was made to forecast whether or not this patient would respond. The predicted effects of the procedure were later correlated with the actual clinical changes. The purpose of the study is threefold :

1. To assess the clinical use of the operation, two questions must be asked : How effective is this in the control of the disease both as regards the proportion of patients helped and the duration of remission obtained ? Secondly, where in the life history of the disease should it be used ? Should it be reserved for the terminal case, or would better results be obtained by its earlier use ?

2. To observe the metabolic changes occurring following the removal of the pituitary gland. This will lead to a better understanding of normal physiology.

3. To follow simultaneously the endocrinological changes and the alterations in clinical course that occur in each patient. In such a way the " mechanisms " governing the progress of this disease may be elucidated.

Although it will be seen that in our hands the palliative results are disappointing, yet we believe that hypophysectomy is a worthwhile effective clinical tool in the treatment of these patients for whom, in the present state of our knowledge, we have nothing better to offer. Furthermore, it is a lever by which knowledge may be gained and thereby the solution to these problems posed by this disease may be found.

THE CLINICAL PROCEDURE

The care of these patients calls for the highest degree of teamwork between general surgeon, neurosurgeon and physician. Dr. Donald Matson has carried out the hypophysectomies and the completeness of the operation, the lack of morbidity and mortality are a tribute to his skill.

Pre-operative care, operative technique and post-operative management

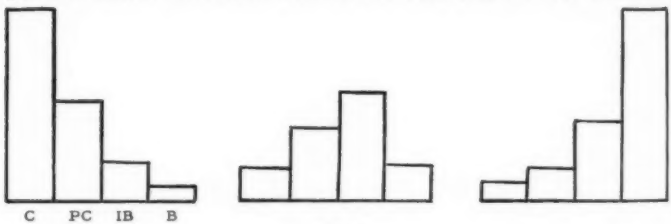
Pre-operative cortisone therapy is supplemented with intravenous compound F during operation. Two hundred milligrams of cortisone is given on the day of operation and this is decreased until the maintenance dose of 50 milligrams of cortisone per day is reached by the seventh post-operative day.

Hypophysectomy is carried out under general anaesthesia through a right frontal approach. The pituitary stalk is cut with a sharp knife immediately above the diaphragm and is traumatized as little as possible. The gland is removed with an extracapsular dissection. In the last half of the series, it has been possible to remove it intact in two-thirds of the cases. All the patients develop diabetes insipidus in the immediate post-operative period. The ultimate patterns which the diabetes insipidus follows will be described later. To avoid the dangers of water intoxication, a complication associated with high fluid intake, large corticoid therapy and simultaneous pitressin therapy, it is now our practice to leave the diabetes insipidus untreated with antidiuretic hormone, but allow unlimited fluid intake for the first week. By that time, in the majority of patients, it will have diminished to such an extent that it does not require treatment. If, however, the polyuria is sufficient to interfere with sleep it can then be treated with pitressin either in the form of pitressin snuff or as pitressin tannate in oil.

All patients require thyroid replacement. Ninety milligrams thyroid extract per day are given starting one month post-operatively.

Complications

These have been few. Anosmia due to olfactory tract damage is the most common and disturbing complication for the patient. No serious neurological complications and no visual disturbances have occurred. Single convulsions have been seen on five occasions and for this reason



Oestrogenic activity

Fig. 3.
" Cortisone effect "

No oestrogenic activity

the patients are maintained on dilantin for six months post-operatively. There has been one wound infection requiring removal of the bone flap. On two occasions signs of raised intracranial pressure have necessitated reopening the craniotomy wounds. A " wet infarct " of the right frontal lobe was found and partial frontal lobectomy carried out. Both these patients did well and it was felt that this complication resulted from a combination of a minor degree of water intoxication associated with the trauma caused by retraction of the lobe.

Results

The critical evaluation of any clinical procedure is always difficult. The results reported here may be of no statistical significance but they do indicate trends in the behaviour of advanced mammary cancer when treated by hypophysectomy. As the biological potential of the tumour as well as the host resistance differ in each case, no two cases can be compared one with the other. Similarly, it is difficult to compare cases reported by other groups of workers. With these reservations understood, certain criteria must be defined before the results can be examined.

Only objective remission has been counted. This consists of visible regression of cutaneous disease, X-ray regression of pulmonary or skeletal disease, or chemical evidence of healing as shown by alterations in urine calcium excretion or serum acid phosphatase levels. A remission ceases with the development of new disease or the progression of pre-existing disease. It should be stated here that on numerous occasions we have seen healing of disease in one area, with simultaneous progression of disease in another ; such a patient would *not* be considered to be in a state of remission.

The results obtained have been graded under the definitions of excellent, fair, and none. By excellent is meant the unequivocal alteration in the natural progress of the disease with healing of metastases. By fair is meant the obvious halting of the disease with subjective but not necessarily objective improvement.

Forty cases of advanced mammary cancer have been treated by hypophysectomy, eleven of these too recently for any valid interpretation of the results to be made. Twenty-nine cases have been followed for more than eleven months or to death and it is these that are reported in Table I. There have been no operative deaths in this series of forty cases.

TABLE I

—	—	Months remission	Months Survival
Excellent	8	10	15+
Fair	11	4½	9+
None	10	0	2½
Total	29		

From Table I it will be seen that 27 per cent. achieved an excellent

result and 38 per cent. had a fair result. Thus, nineteen out of twenty-nine or 65 per cent. had the progress of their disease favourably altered by the operation. This figure is comparable to those figures reported in other series throughout the world. It is interesting to note than when patients showed no response to hypophysectomy, the survival time was only two and a half months. This indicates that at least in these ten cases the operation is being performed at the very end of the natural history of the disease. It is necessary that this policy should be adopted when any experimental procedure is under therapeutic trial. It is our growing belief that hypophysectomy should be used earlier than it has been used in our series to date. Additional support for this concept may be seen if the results are re-examined in a different light. If the cases are divided into two groups, one termed " early " and the other " late," the results are seen in Table II. By " late " is meant that the patient has advanced skeletal and visceral disease affecting the lungs, liver or brain. By " early " is meant that cutaneous metastases are limited or skeletal lesions few.

TABLE II

—	—	Months remission	Months survival
" Early "	12	7½	8½
" Late "	17	2	5
Total	29		

The difference between remission and survival times in the two groups is obvious. Although there was objective evidence that the clinical course of many of the patients had been altered favourably by hypophysectomy, yet it could be argued that the difference in remission and survival times between the two groups is due to the extent of the disease and not to the response of each group to hypophysectomy, those patients with more advanced disease dying sooner than those with less disease. It is interesting to see in the early group that although survival is still relatively short, the period of remission is almost as long. This may indicate that natural progression of the disease has been altered in a fundamental and important way. It would appear that the disease is halted and controlled for a period of time and that there is then a sudden " escape," when it assumes a fulminating course which rapidly leads to death. This will be further discussed.

Selection

Although much work has been done in this field, as yet no reliable method of selection has been established. Indications that the tumour is still responsive to hormonal stimulation and hence will benefit from hypophysectomy may be gained in the following manner :

1. Previous response to hormonal therapy. Previous improvement from oophorectomy or cortisone therapy is a favourable sign. However, there may

be a group of patients who will respond to hypophysectomy who will have shown no previous response to either of these other manoeuvres.

2. With the use of "stimulation" or "suppression tests" and the simultaneous observation of either the urine calcium excretion or the serum acid phosphatase levels. Urine calcium excretion studies have been used extensively in our series in patients with osseous metastases. A positive response to either test is a strong indication that hypophysectomy will be successful. A negative test does not, however, preclude a successful result.

An example of the use of these methods of selection is given later.

THE METABOLIC CHANGES

Water

Damage to the pituitary stalk and supraoptic and paraventricular nuclei at hypophysectomy leads to diabetes insipidus in all cases. These patients have an inability to concentrate their urine and the daily volumes are in excess of 2,500 cc. per day. The severity and permanency of the diabetes insipidus is proportional to the trauma to which the neurohypophyseal mechanism is subjected. Damage of the hypophyseal cells may be due to direct trauma, temporary oedema at the operative site, retrograde neuronal degeneration from the cut end of the stalk or to any combination of all these. Permanent diabetes insipidus requiring continuous pitressin therapy was seen only when either the stalk had been invaded with metastatic tumour or had been clipped and cauterized. Simple sharp stalk section with a knife, although not reducing the incidence of immediate post-operative diabetes insipidus, did eliminate the severe persistent form.

Three distinct patterns of diabetes insipidus have been encountered:

1. *The severe form.* The immediate polyuria of 7,000 to 9,000 cc. per day falls slightly to a range of 5,000 to 6,000 cc. per day which persists at this level. The high urine volumes require pitressin therapy.

2. *The diphasic response.* The initial polyuria is followed by a five to seven day period of urine volumes of approximately 3,000 cc. per day and these then rise to permanent levels of 4,000 to 5,000 cc. This is the least common variety. A possible explanation for this form may be that the initial diabetes insipidus is due to direct trauma and oedema of the hypothalamic nuclei. This is followed by a period of reduced urine volumes when the oedema subsides and previously formed ADH escapes into the circulation. The final phase of increased polyuria being permanent is due to the retrograde degeneration of cells in the nuclei.

3. *The commonest variety.* Here the initial polyuria, which may be very great (one patient excreted 29,000 cc. in the first day) subsides until, by about the seventh day, the volume ranges between 2,000 to 3,000 cc. per day. This variety of diabetes insipidus is subclinical but nevertheless it can be demonstrated that there is a disturbance of normal homeostatic mechanisms. Evidence for this is seen in that random serum osmolarities on these patients show raised levels from the normal 286 milliosmoles per litre to the post-hypophysectomy level of 296 to 305 milliosmoles per litre.

Comment

1. We have been unable to confirm the contention that the severity of diabetes insipidus is proportioned to the cortisone dosage rate (Ikkos, *et al.*, 1955). In only one patient has it been possible to discontinue

cortisone therapy without an Addisonian crisis ensuing. In this patient after eight days, the polyuria and the pitressin need had shown no reduction.

2. One patient, hypophysectomized in pregnancy, developed diabetes insipidus which was uncontrollable with pitressin. Post-partum, the polyuria decreased and pitressin was no longer required. At this time, the response to pitressin therapy was normal. It is believed that both endogenous and exogenous antidiuretic hormone were being destroyed by a placental hormone (Eglin and Jessiman, 1958).

Aldosterone

Aldosterone excretion was measured by a modification of the method of Neher and Wettstein (Neher and Wettstein, 1956; Hernando, *et al.*, 1957). Four patients were studied and the detailed results are reported elsewhere (Ross, *et al.*, 1957).

These indicate that :

1. In the immediate post-operative period, aldosterone is excreted at levels greater than normal.

2. The twenty-four hour excretion values are related to the degree of diabetes insipidus. The initial post-operative polyuria is accompanied by the maximal rise in aldosterone excretion. The hormone levels fall as the diabetes insipidus diminishes or pitressin therapy is used to reduce the urine volume. In one of our patients four and a half months after hypophysectomy, in whom the urine volume was controlled with twice daily inhalation of pitressin snuff, the aldosterone excretion level was normal. Withdrawal of pitressin led to urine volumes of 5,000 to 6,000 cc. per day and the aldosterone excretion was quadrupled. The lowest recorded aldosterone excretion rate in these patients was in a patient who developed minimal diabetes insipidus.

3. The use of long-term cortisone does not inhibit the aldosterone excretion. One patient had been on cortisone at the dose level of 75 milligrams per day for one year prior to hypophysectomy and at 400 milligrams per day for one week prior to hypophysectomy. In the post-hypophysectomy period with the development of diabetes insipidus, the aldosterone excretion showed the expected rise.

Comment

1. These observations support the concept that the regulation of aldosterone secretion is mediated from centres outside the pituitary, possibly hypothalamic in position. It is felt that these cases show the control of the secretion of aldosterone is possibly related to volume changes caused by the diabetes insipidus.

2. Autopsy findings in the adrenal glands are of interest. It has been suggested that aldosterone is secreted by the zona glomerulosa of the adrenal cortex (Giroud, *et al.*, 1956) and that oestrogen secretion is one function of the zona fasciculata and zona reticularis. After hypophysectomy these patients show extreme atrophy of the zona fasciculata and reticularis whilst the zona glomerulosa appears normal.

Thyroid studies

The radio-active iodine uptake per twenty-four hours was measured over the thyroid gland using a scintillation counter after 5 to 10 microcuries

I^{131} had been given by mouth. Serum levels of protein bound iodine were measured by a modification of the method of Zak (Zak, 1952). Normal levels for the euthyroid patient obtained in our laboratory are I^{131} 15 to 50 per cent. uptake per twenty-four hours and serum protein bound iodine 4 to 8 micrograms per cent. Depression of thyroid function was demonstrated by the reduction of the pre-operative radio-active iodine level of a mean of 30 per cent. uptake per twenty-four hours to a post-operative mean of 5 per cent. per twenty-four hours. A comparable fall in protein bound iodine levels was seen from a pre-operative mean level of 6 micrograms per cent. to a post-operative level of 2 micrograms per cent.

Follicle stimulating hormone

FSH was measured on twenty-four hour collections of refrigerated urine by the mouse uterine weight method of Klinefelter and Albright (Klinefelter, *et al.*, 1943). The lowest detectable level is 2.5 m.u. The range for a normally menstruating woman is 10 to 20 m.u.; these levels become positive to 100 to 300 m.u. per twenty-four hours after the menopause. Many of the patients in the pre-hypophysectomy period showed post-menopausal levels. Contrary to our expectations and in support of the work of others (Lemon, 1957 ; Sohval and Soffer, 1951), we observed that those patients who had been on prolonged and, at times, high doses of cortisone (200 to 400 milligrams per day) did not show a reduction in their FSH values and indeed might show levels higher than would have been expected. After hypophysectomy, it took from one to ten weeks for the FSH levels to drop to a base line level, 2·5 m.u. with an average time being one to two weeks.

Comment

Both thyroid studies and FSH measurements were used as endocrinological methods of measurement of the completeness of hypophysectomy. A close correlation could be made between these determinations and the findings in the sella turcica in those patients coming to autopsy. One patient who obtained nine and a half months excellent clinical remission did not require thyroid extract and showed an I^{131} uptake of 51 per cent. per twenty-four hours in the post-hypophysectomy period. At autopsy a rim of cells one cell thick was found in one corner of the sella turcica. These cells stained positive with periodic acid Schiff stain and it is probable that they were secreting thyrotropic hormone.

Urine oestrogens

A sensitive, accurate, chemical method of measuring urine oestrogens is desirable. Such a method is not available. The Brown technique (Brown, 1955) fills these requirements most closely. However, this technique even with the addition of the saponification modification (Brown, 1957) is not accurate at levels of less than 2.5 micrograms per twenty-four hours of oestradiol, oestrone, and oestriol. Many of these women who are post-

menopausal or who have been castrated, are secreting one microgram or less of these components each day, levels at which the Brown technique is inaccurate. Furthermore, we believe that the chemical methods will measure only a proportion (20 to 30 per cent.) of the total urine oestrogens or the oestrogenic metabolites. It is the " overall " oestrogenic activity that we assume to be relevant and important in the stimulation of mammary cancer. It is for these reasons that we have employed methods which measure the total biological oestrogenic activity of the urine.

Smith and Smith Bio-assay (Smith, O. W. and Smith, G. V. 1952)

This is a modification of the Alan-Doisy technique. Oestrogenic activity is measured by observing the vaginal smear changes in spayed adult female rats. The seventy-two hour specimen of urine is divided into two aliquots, the first is treated by a ten minute acid hydrolysis and the second subjected to a three-hour acid hydrolysis in the presence of zinc. The results of the straight acid hydrolysis are expressed as the T_o activity of the urine and represents the summation of the activity of oestrone, oestriol and oestradiol present. The T_{zn} fraction is that fraction liberated by the zinc hydrolysis and recent work suggests that this fraction represents oestrogen precursors or intermediate metabolites of oestrogens. The lowest detectable levels are T_o 50 i.u. and T_{zn} 100 i.u., levels equivalent to 0.5 micrograms and 1.0 microgram of oestradiol 17 β respectively. Normally, the high pre-menopausal levels which fluctuate with the menstrual cycle fall to these levels in the post-menopausal period.

Cytology techniques

Two techniques have been used :

Vaginal smear. Vaginal cytology is obtained from the posterior fornix and stained in the routine Papanicolaou technique. A cell count is made and the cells divided into cornified, pre-cornified, intermediate basal, and basal types. This technique is simple and reliable. The presence of cornified and pre-cornified cells indicates oestrogenic activity whereas intermediate basal and basal cells indicate lack of oestrogenic stimulation. We have observed a third pattern in which intermediate basal and pre-cornified cells preponderate. We term this a " cortisone effect " (Fig. 3). Its explanation is uncertain but it may be due to a direct action of the cortisone on the vaginal mucosa or to conversion or degradation products of cortisone influencing the cytology.

Urethral cytology. A smear made of the sediment obtained from the centrifugation of an early morning specimen of urine shows the presence of urethral cells. These cells range from nucleated or non-nucleated, the higher the percentage of the latter, the greater the degree of oestrogenic activity. Dr. Castellanos, who is carrying out this study, has evidence that the presence of these cells is due to oestrogens of adrenal rather than ovarian origin and furthermore is contingent on high FSH levels. If this is the case, it is an interesting example of crossed hormonal stimulation.

Using these techniques, the results obtained have shown that :

1. Many patients coming to hypophysectomy had no evidence of oestrogenic activity. However, oestrogens were demonstrated by all these methods of assay. Thus the bio-assay (Smith and Smith, 1952) technique showed measurable oestrogens in eight out of twelve cases studied. The vaginal smear technique showed an oestrogenic smear in thirteen out of eighteen cases. The urethral cytology technique showed the presence of oestrogens probably adrenal, in eight out of ten cases. Of the remaining two cases, one had been castrated only ten days previously and thus insufficient time had elapsed for increased amount of adrenal oestrogens to appear and in the second, the patient had been on a prolonged course of cortisone and thus adrenal oestrogen production had been suppressed.

2. Post-hypophysectomy oestrogen determinations showed a reduction of all oestrogenic activity to baseline levels in those patients showing previous activity. No oestrogens could be detected by the bio-assay technique in the early post-operative period. Using the vaginal smear method, a basal cell atrophic smear was recorded within three to four weeks. The urethral cytology count of non-nucleated cells fell from the pre-operative average of 50 to 60 per cent. to a post-operative level of 5 to 8 per cent. by the fifteenth post-operative day.

3. A return of oestrogenic activity was measured in six patients. This resurgence of oestrogens was frequently seen in association with the occurrence of a fulminating exacerbation of the disease. It was measured both by the bio-assay and vaginal smear techniques.

Comment

In one post-hypophysectomy patient being treated with 19-norepitestosterone oestrogens were measured by countercurrent distribution. Daily excretion of oestradiol 17 β 30.2 micrograms and oestrone 10.0 micrograms per day were recorded. This evidence of conversion of testosterone to oestrogen was accompanied by a clinical worsening of the disease.

A composite picture of the type of study carried out on these patients showing the clinical and metabolic changes that occur is well illustrated by the following case :

Case III. Mrs. H. J. (PBBH unit #3K879) was thirty-three years of age when in February 1952 she noted a lump in the left breast. In March 1952 a left radical mastectomy was carried out. The axillary glands were not involved. She remained well until August 1955, when she was found to have osseous metastases. These were treated with X-ray therapy and she was placed on testosterone propionate 100 milligrams i.m. twice weekly starting in October 1955. On this therapy, her symptoms improved and her disease was halted until June 1956, when once again she developed bone pain. Further X-ray therapy was carried out but by November 1956, it was felt that this therapeutic measure could no longer be used and that the disease was progressing.

She was admitted to the Peter Bent Brigham Hospital for the first time on 9th December 1956. Physical examination revealed her general condition to be good but she was obviously in considerable pain. No local recurrences could be detected and examination of the abdomen revealed no hepatic enlargement

and no masses were palpable. Preliminary investigations at this time revealed urine oestrogen T_o 55 i.u., T_{zn} 110 i.u. Urine calcium excretion ranged between 260 and 370 milligrams per twenty-four hours. Vaginal smear was atrophic showing 85 per cent. basal cells. To establish whether or not this tumour was hormone stimulated, an oestrogen stimulation test was carried out on 11th December 1956. Stilboestrol 10 milligrams was administered on two successive days. By the end of the second day, she had had such severe systemic reaction that the dose of stilboestrol for the succeeding day was cancelled. She was experiencing bone pain, malaise, nausea and was pyrexial. Over the ensuing week, her urine calcium excretion rose to 750 milligrams per twenty-four hours. Her vaginal smear, under the influence of the administered stilboestral, became oestrogenic in type. She was discharged over Christmas and re-admitted on 28th December 1956. Investigations carried out at this time showed a urinary FSH positive 200 m.u. per twenty-four hours, the persistence of an oestrogenic vaginal smear, and thyroid function studies showing an I^{131} uptake of 35 per cent. per twenty-four hours and PBI 7.4 micrograms per cent. The urine calcium had fallen to 200 milligrams per day. On 29th December 1956, an ovariectomy was carried out. Exploration of the abdomen revealed no liver metastases and the ovaries that were removed were atrophic and the histology was compatible with that to be expected following an X-ray castration. She experienced no improvement in her bone pain and her urine calcium did not fall.

On 2nd January 1957 she underwent hypophysectomy. Her bone pain was relieved immediately and she was discharged from hospital on her seventeenth post-operative day. In the immediate post-operative period, she developed diabetes insipidus with daily urine outputs ranging from 6,000 to 8,900 cc. per day. Pitressin therapy was withheld until the eighth post-operative day at which time pitressin snuff was administered. This produced a fall in her urine volumes to a range of 3,000 to 3,500 cc. per day. Study of her aldosterone excretion at that time showed a rise which closely paralleled the changes seen in her water excretion. On the first and third post-operative days, 28 micrograms of aldosterone were excreted. With the administration of pitressin and the control of her diabetes insipidus, the aldosterone output fell until by 13th January 1957 (the eleventh post-operative day) the aldosterone excretion was 2 micrograms per twenty-four hours. The urine calcium excretion which had remained constant in the range of 200 milligrams per day before and ofter ovariectomy fell immediately in the post-hypophysectomy period to low normal values of about 100 milligrams per day. Urinary FSH was negative to 5 m.u. Thyroid function studies showed a satisfactory reduction, I^{131} 9 per cent. per twenty-four hours, PBI 2.2 micrograms per cent., and the vaginal smear showed a slow change towards a basal cell type.

She remained well and was able to lead an absolutely normal life for the next four and a half months, at which time she was re-admitted to hospital for investigations. There was no clinical evidence of exacerbation of the disease. Investigations showed urinary FSH negative to 2.5 m.u. Urine calcium remained low in a range of 50 to 100 milligrams per day and the vaginal smear was basal in type. Thyroid function studies showed I^{131} uptake 14 per cent. per twenty-four hours, and PBI 7 micrograms per cent., the raised PBI level being a reflection of the thyroid therapy that she was receiving at that time. A study of her aldosterone excretion was carried out. On admission, the patient was taking pitressin snuff to control her moderate diabetes insipidus. Whilst taking this medication, her urine volumes ranged between 2,300 cc. and 3,000 cc. per day. On 16th May 1957 the pitressin snuff was discontinued and her urine volume rose to range between 5,500 and 6,500 cc. per day. This was associated

with a rise in aldosterone excretion from 5 micrograms to 22 micrograms per twenty-four hours. She was discharged from hospital on 2nd June 1957. She remained well until 20th July 1957. At this time she developed abdominal distension, nausea, and pain in her bones. This sudden deterioration in her condition necessitated her admission to hospital on 2nd August 1957. On admission, she was found to be semi-comatose. She was jaundiced and examination of the abdomen revealed the presence of ascites and an enlarged liver. She had bilateral pleural effusions. Investigations revealed a raised urine calcium excretion which was in the range of 300 to 570 milligrams per twenty-four hours. A vaginal smear showed a shift towards an oestrogenic pattern when compared to the smear taken three months previously and a urine oestrogen excretion T_o 50 i.u., T_{2n} 320 i.u. Despite increased corticoid therapy, she went rapidly downhill and died on 15th August 1957. Autopsy findings revealed no evidence of any hypophyseal tissue in the sella turcica. The adrenal glands showed marked diminution in the zona fasciculata and a normal zona glomerulosa. The liver showed large areas of tumour infiltration so widespread that normal liver architecture could not be recognised. The clinical and metabolic changes that have been described are illustrated in Figs. 4, 5, 6, 7 and 8.

The conclusions that one may draw from this study are :

1. The clinical course of this patient was modified by hypophysectomy. She obtained an excellent remission for seven and a half months and at the end of that time underwent a fulminating exacerbation of her disease which had a mainly hepatic component.

2. With the use of a stimulation test and urine calcium excretion studies, it was possible to determine that this patient had a hormone stimulated tumour and to predict that she would respond well to hypophysectomy.

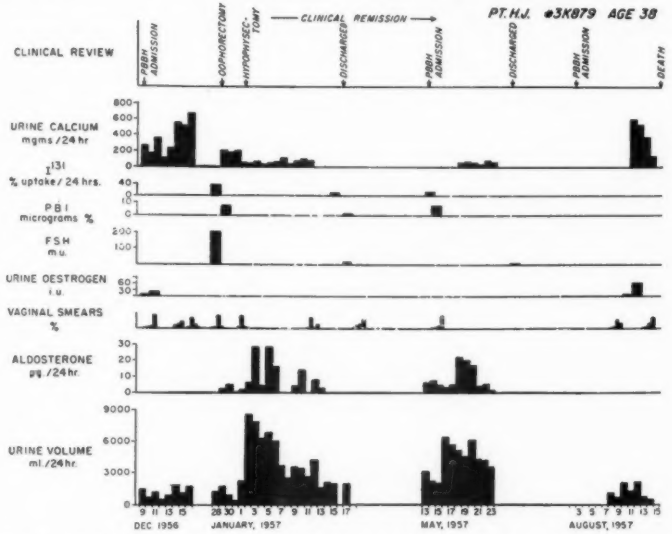


Fig. 4. Patient H. J. A representative chart showing the type of clinical and metabolic study carried out on patients undergoing hypophysectomy. The individual components of the study will be examined in the ensuing figures.

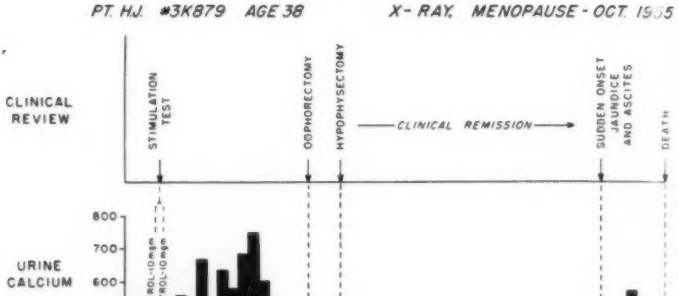


Fig. 5. Patient H. J. Urine calcium excretion study. The hypercalcuria seen following the stimulation test indicated that this tumour was hormone stimulated. The failure of the urine calcium to fall following oophorectomy suggested that stimulation of the disease was not due to ovarian hormones. The prompt fall following hypophysectomy indicated that a pituitary stimulating factor had been removed.

3. Endocrinologic evidence of the completeness of hypophysectomy was obtained by the observation of satisfactory falls from the pre-operative levels of FSH, radio-active iodine uptake, and protein-bound iodine levels to post-operative basal levels. Autopsy findings showed the absence of pituitary tissue in the sella turcica and confirmed these endocrinologic studies.

4. In the absence of the pituitary, it was shown that this patient was capable of secreting large quantities of aldosterone and that this was related to the degree of diabetes insipidus. It is interesting to note that autopsy examination of this patient's adrenal glands showed persistence of the zona glomerulosa and atrophy of the zona fasciculata and zona reticularis.

5. A simultaneous examination of the urine oestrogen excretion, vaginal cytology and urine calcium excretion showed that prior to hypophysectomy when the patient was in a state of exacerbation with rapidly advancing disease, there was no oestrogenic stimulation present. Further the urine calcium did not fall nor did the patient's symptoms improve following oophorectomy. Complete relief of bone pain and a fall in urine calcium levels were seen in the immediate post-operative period and persisted. This would tend to indicate that this tumour was under stimulation by some direct pituitary factor.

6. A resurgence of oestrogenic activity was measured by the bio-assay technique in the terminal state. The activity was seen in the T_{zn} fraction and was related to the clinical development of extensive hepatic involvement with secondary metastatic disease.

A study such as this enables the course of the disease and the effects of treatment to be followed. The physiologic changes in metabolism have been observed and the endocrinological changes associated with the final

exacerbation lead us to consider the mechanisms which may have been responsible.

MECHANISMS

The understanding of the mechanisms underlying and governing tumour growth and development proceeds in phases. New facts concerning either the host-background or the tumour itself are brought to light by technical improvements in methods of study. The intelligent interpretations of these facts and their correlation with the clinical aspects of the disease is essential if progress in treatment is to advance.

The hormonal milieu surrounding the cancer cell is of paramount importance to the growth of cancer of the breast. When it is disturbed, alteration in growth rate may be seen. This may decrease and a remission is obtained or it may increase and an exacerbation follows. This alteration may occur naturally, as with the menopause, or as a therapeutic measure planned by the clinician. It is the duty of the clinician to use these measures with caution choosing the appropriate time for their use and realizing that unwise meddling may lead not to the desired remission, but possibly to an exacerbation (Wilson, *et al.*, 1958).

The hormonal influences affecting the normal mammary gland and also mammary cancer are extremely complex. The original premise that it was the ovarian hormones, primarily oestrogens, that were of sole importance,

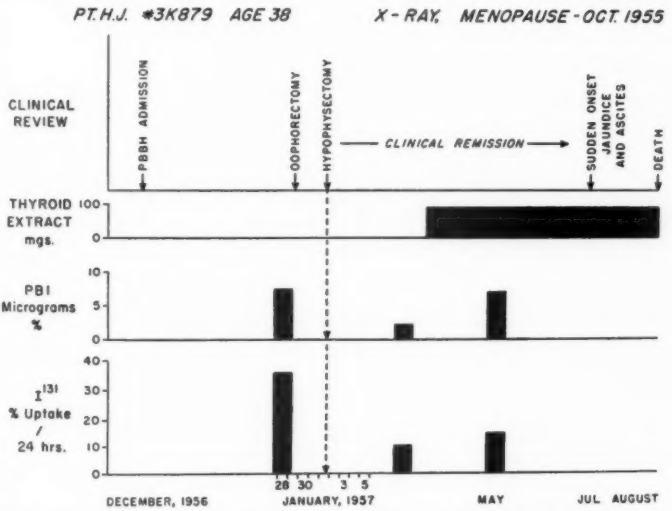


Fig. 6. Patient H. J. Thyroid function studies. Before hypophysectomy the levels were normal. After hypophysectomy a satisfactory fall is seen in both I^{131} uptake and PBI levels. The raised PBI level in May 1957 is the result of her thyroid replacement therapy.

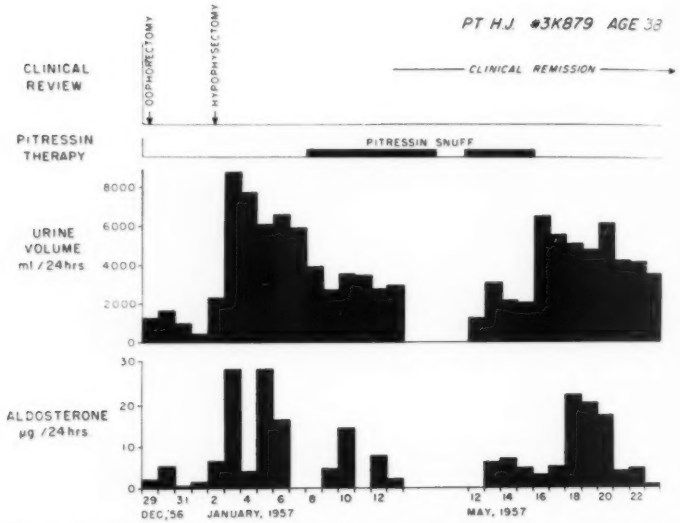


Fig. 7. Patient H. J. Aldosterone excretion study. Diabetes insipidus developed on the first day following hypophysectomy and was associated with a rise in aldosterone excretion. With the use of pitressin snuff, the urine volume was reduced and this was accompanied by a return of aldosterone excretion to normal. In May 1937, whilst on pitressin snuff, urine volumes and aldosterone excretion were normal. Withdrawal of the pitressin snuff led to polyuria and a concommitant rise in aldosterone excretion.

has given way to more complex theories. Adrenal and thyroid hormones are recognized for their importance and recently the influence of pituitary factors has been assuming a dominant role. It must be realized, however, that countless unidentified and un-named hormones and their intermediate metabolites form a background for tumour growth. During the last three years, five new oestrogens have been isolated and identified and six other oestrogenic substances characterized but not identified other than to demonstrate that they are not the same as these recently identified oestrogens (Smith and Smith, 1958). Little, as yet, is known of their effect on mammary cancer. A scheme of the hormonal influences on mammary cancer might be depicted as shown in the diagram (Fig. 9).

Assuming the theory of the importance of " milieu disturbance " as being correct, the reasons for the success of hypophysectomy fall into two groups :

(*a*) Absolute removal of the stimulating factors, growth hormone, lactogenic hormone and, through indirect action on target glands, of oestrogens, progesterone, and thyroid hormone.

(*b*) Partial removal of stimulating factors. This would account for the successes seen with incomplete hypophysectomy, stalk section or irradiation of the sella turcica. Study of our own series and of those of others (Luft, *et al.*, 1957) shows

that although the duration of remissions may not be as long, some of the best results have been obtained with incomplete removal of the gland.

Failure of hypophysectomy

It is in the study of these cases that much may be learned. They fall into two groups :

(*a*) Those in which the tumours showed no response at any time. This included 35 per cent. of our cases.

Tumour autonomy. The existence of true autonomy of tumour growth has already been discussed and the possibility of such an entity cannot be denied.

Extent and rate of growth of disease. There is little doubt that the "late" case with massive visceral metastatic involvement in essential organs has passed beyond the point at which hormonal measures can bring about a reversal of the natural progress of the disease. Similarly, if the disease has assumed a fulminating downhill course, the relatively slowly acting endocrine ablation procedure will be unable to act rapidly enough to prevent a fatal outcome.

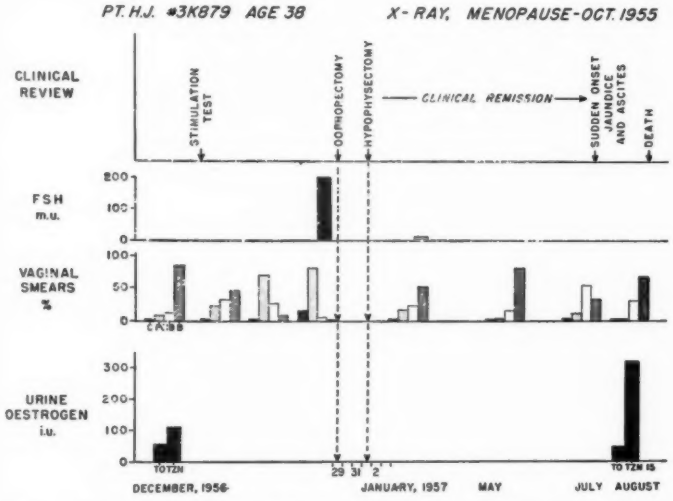


Fig. 8. Patient H. J. Follicle stimulating hormone, vaginal smear and urine oestrogen study. Prior to hypophysectomy the FSH and urine oestrogen levels were in the post-menopausal range. The vaginal smear, initially indicating no oestrogenic stimulation, became pre-cornified following the stimulation test. Following hypophysectomy no FSH excretion could be detected. During the period of clinical remission the vaginal smear became atrophic. The sudden exacerbation of disease was associated with an increase in urine oestrogen excretion seen in the T_{Zn} fraction and a change in the vaginal smear suggesting oestrogen stimulation.

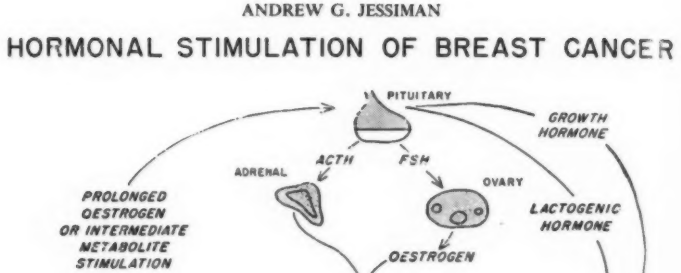


Fig. 9.

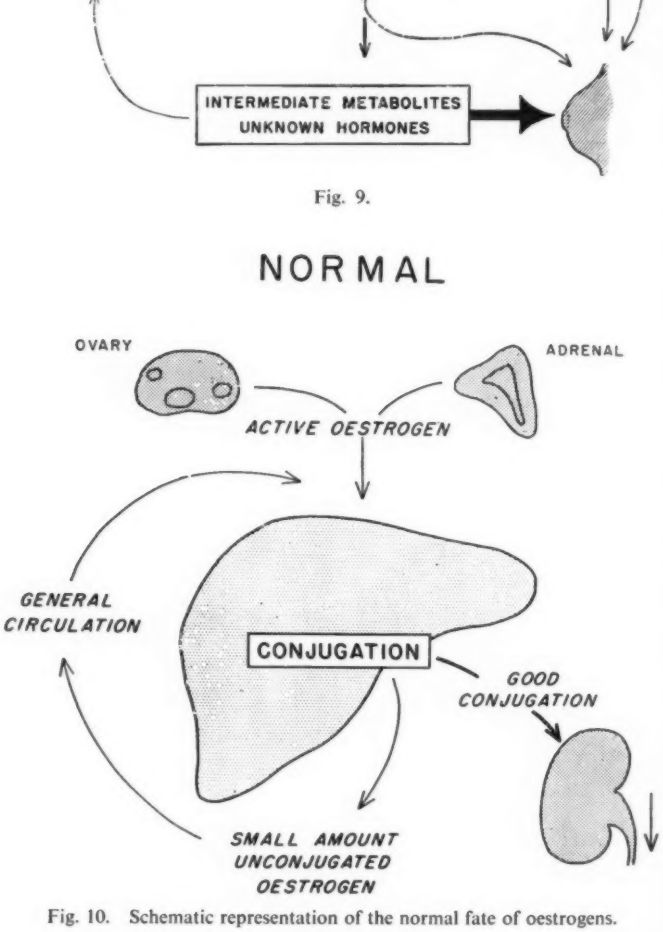


Fig. 10. Schematic representation of the normal fate of oestrogens.

(*b*) Those in which the tumour responds initially but after a period of remission, undergoes an exacerbation.

Associated with incomplete hypophysectomy. The initial depression of function of the remaining cells, as already stated, may lead to a remission. However, in time, previous hormonal levels are re-established and once again tumour growth is stimulated.

Associated with complete hypophysectomy. Experimental work in animals has shown that metastatic tumours are composed of a mixture of cells showing all degrees of responsiveness to hormone stimulation. If such is the case in mammary cancer, a remission occurs when the hormone stimulated cells degenerate following hypophysectomy. The duration of this remission depends on the length of time that it takes for the relatively or totally unresponsive cells to gain ascendancy and cause an exacerbation. A comparable situation is seen in the radiosensitivity of tumours in which the cells of any one tumour will show a differential sensitivity to irradiation. A second, and more attractive explanation may be that the tumour, which has maintained its hormone dependency, is restimulated by a resurgence of hormones. The presence of oestrogens in the oophorectomized, adrenalectomized and hypophysectomized patient has been widely reported in the literature and has been confirmed by observation of our own cases. In developing a thesis as to the mechanism by which the presence of these hormones, often in small quantities, may activate disease two other observations made on our cases should be noted. The " all or none " law of metastatic response to hormonal therapy is not true. On many occasions we have seen healing of metastases of one variety in one area associated with a simultaneous advance of disease in another. The common pattern is of healing of skeletal or cutaneous metastases at the same time as hepatic metastases are growing rapidly. Also we have observed that the final fatal exacerbation, after a period of remission, often runs a fulminating course frequently with a preponderant hepatic component.

These facts may be explained by a local sensitivity and responsiveness of tumour cells, already present, to a return of hormones. When hepatic metastases are present, this explanation is particularly acceptable. The normal metabolism of oestrogens in these women is disturbed. An example of this is that they excrete a higher proportion of oestriol to total oestrogens in the urine (Brown, 1957). Also we have seen that the urinary T_{zn} fraction, believed to be oestrogen precursors or intermediate metabolites of oestrogens, is the first oestrogenic component to reappear. The return of this active oestrogenic principle, even in small amounts, can be expected to be most effective in stimulating the disease in the liver. Here, where the normal inactivation of oestrogens by conjugation occurs, a high concentration of oestrogens may build up and this sets off a vicious circle in which growing metastases damage contiguous hepatic cells and decrease normal hepatic function. This leads to failure of conjugation of

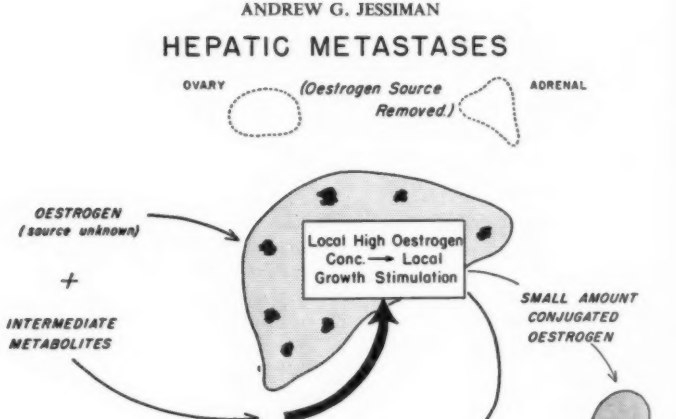


Fig. 11. Schematic representation of the fate of oestrogens in a patient with hepatic metastases.

the oestrogens arriving in the portal blood stream and a further stimulation of the disease (Figs. 10 and 11).

The enigma as to the source of these oestrogens in these patients is, as yet, unanswered. Are they made by undetectable ovarian or adrenal nests? Does the tumour itself make oestrogens and thus ensure self propagation? Is the cortisone used in replacement converted into oestrogens? Does the patient's food contain oestrogens or perhaps substances which the deranged hepatic function converts into oestrogens? At the present time it is not possible to answer these questions but much work is currently being done and must be done in this field in the future. Advances in methods of study are needed so that not only may the pituitary factors, growth hormone and lactogenic hormone be measured with accuracy, but also that a detailed study may be made of the unexplored field of the intermediate metabolites of oestrogens.

CONCLUSIONS

1. The rationale for hypophysectomy has been discussed, the importance of a pituitary factor acknowledged and evidence produced suggesting that this may be growth hormone.

2. As part of a larger study of metastatic mammary carcinoma currently being carried out at the Peter Bent Brigham Hospital, forty patients have been treated by hypophysectomy. Studies of these cases have been carried out to assess the clinical use of this procedure as a therapeutic tool and also as a means of obtaining further knowledge as to governing factors in growth rate of the disease itself.

3. The problem of widely differing response of individual patients to hypophysectomy has been illustrated by two cases.

4. The clinical indications, operative technique, complications, methods of selection and results have been described.

5. Metabolic alterations of thyroid function and of the excretion of water, aldosterone, follicle-stimulating hormone and oestrogens were observed. In some instances these have led to a better understanding of the normal physiological role of the pituitary gland.

6. Theories have been advanced as to the mechanisms governing the response to hypophysectomy. It has been postulated that hormonal "milieu disturbance" is the most important factor and that the response obtained depended on the relative hormone sensitivity of the tumour mass as a whole. The importance of hormone resurgence and the origin of these hormones is still debatable.

7. Much further work must be done in methodology to enable a more accurate assessment to be made of the endocrinological background of the tumour. Study of the many unidentified hormones and intermediate metabolites of hormones is needed with particular reference to their action on the growth rate of mammary cancer.

ACKNOWLEDGMENTS

In conclusion, I wish to thank all those of my colleagues whose help has made this work possible.

Sir Stanford Cade, whose vast knowledge of the disease first stimulated my interest.

Dr. Francis D. Moore, whose guidance and encouragement are a continuing support.

Dr. George Smith and Dr. Olive Smith, from whom I have learned of the endocrinological background of the disease.

Drs. Donald Matson, Kendall Emerson, Herbert Selenkow, Walter Van't Hoff and other members of Harvard Medical School who have helped in the care of the patients.

And finally the patients themselves who, by their courage and faith, give strength to those who tend them.

REFERENCES

ATKINS, H. J. B. (1958) in *Endocrine aspects of breast cancer*, edited by A. R. Currie. Edinburgh, Livingstone.
BEATSON, G. T. (1896) *Lancet* **2**, 104, 162.
BROWN, J. B. (1955) *Biochem. J.* **60**, 185.
———— BULLBROOK, R. D., and GREENWOOD, F. C. (1957) *J. Endocrin.* **16**, 49.
———— (1957) in *Endocrine aspects of breast cancer*, edited by A. R. Currie, Edinburgh, Livingstone.
EGLIN, J. M., and JESSIMAN, A. G. (1958) In preparation.
EHNI, G., and ECKLES, N. (1958) Personal communication.
EVERETT, J. W. (1958) Personal communication.
FURTH, J. (1957) *Cancer Res.* **17**, 454.
GIROUD, C. J., STACHENKO, J., and VENNING, E. H. (1956) *Proc. Soc. exp. Biol. (N.Y.)* **92**, 154.

HALL, T. (1958) Personal communication.
HERNANDO, L., CRABBÉ, J., ROSS, E. J., REDDY, W. J., RENOLD, A. E., NELSON, D. H., and THORN, G. W. (1957) *Metabolism* **6**, 518.
HOME, E. (1810) *Lectures on comparative anatomy: in which are explained the preparations in the Hunterian Collection.* Lecture No. 4, London: Longman, Hurst, Rees, Orme and Brown, 1823.
IKKOS, D., LUFT, R., and OLIVECRONA, H. (1955) *J. clin. Endocr.* **15**, 553.
KLINEFELTER, H. F., JR., ALBRIGHT, F., and GRISWOLD, G. C. (1943) *J. clin. Endocr.* **3**, 529.
LEMON, H. M. (1957) *Ann. intern. Med.* **46**, 457.
LUFT, R., OLIVECRONA, H., IKKOS, D., NILSSON, B. L., and MOSSBERG, H. (1957) in *Endocrine aspects of breast cancer*, edited by A. R. Currie. Edinburgh, Livingstone.
LYONS, W. R., JOHNSON, R. E., COLE, R. D., and LI, C. H. (1955) in *Hypophyseal growth hormone, nature and actions*, edited by R. W. Smith, O. H. Gaebler and C. N. H. Long. New York and London, McGraw-Hill.
NEHER, R., and WETTSTEIN, A. (1956) *J. clinl Invest.* **35**, 800.
PEARSON, O. H., LI, M. C., MACLEAN, J. P., LIPSETT, M. B., and WEST, C. D. (1955) *J. Amer. Med. Ass.* **159**, 1701.
——— LIPSETT, M. B., GREENBERG, E., and RAY, B. S. (1957) Abstract presented at the thirty-ninth Annual Meeting of the Endocrine Society.
RAY, B. S., and PEARSON, O. H. (1958) in *Endocrine aspects of breast cancer*, edited by A. R. Currie. Edinburgh, Livingstone.
ROSS, E. J., VAN 'T HOFF, W., CRABBÉ, J., and THORN, G. W. (1958) In preparation.
SMITH, O. W. (1944) *Endocrinology* **35**, 146.
——— and SMITH, G. V. (1952) *Recent Progr. Hormone Res.* **7**, 209.
——— (1958) *Acta Endocr.* (*Kbh.*) In press.
SOHVAL, A. R., and SOFFER, L. J. (1951) *J clin Endocr.* **11**, 677.
WILSON, R. E., JESSIMAN, A. G., and MOORE, F. D. (1958) *New Engl. J. Med.* **258**, 312.
ZAK, B. (1952) *Analyt. Chem.* **24**, 1345.

SAYINGS OF THE GREAT

" Those who have dissected or inspected many bodies have at least learned to doubt ; when others, who are ignorant of anatomy and do not take the trouble to attend to it, are in no doubt at all." *Morgagni.*

" Those who can, do ; those who cannot, teach." *Anon.*

" Genius, like the inhabitants of the depths of the sea, moves by its own light." *Ramon y Cajal.*

" This is the way physicians mend or end us
Secundum artem ; but although we sneer
In health—when ill, we call them to attend us,
Without the least propensity to jeer ;
While that hiatus maxime deplendus
To be fill'd by spade or mattock, 's near,
Instead of gliding graciously down Lethe,
We tease mild Baillie, or soft Abernethy."

Lord Byron.

Contributions are invited.

ON THE NATURE AND TREATMENT OF WOUND SHOCK

Lecture delivered at the Royal College of Surgeons of England
on
14th June 1958
by

Ruscoe Clarke, F.R.C.S.
Consultant Surgeon Birmingham Accident Hospital

during a Symposium on Shock and Allied Phenomena held by the Faculty of Anaesthetists

I HAVE USED the term " wound shock " deliberately with three objects in view. Firstly to make it clear that I am discussing the condition that follows injury rather than any abstract general concept of " shock." Secondly because it provides an excuse for the invasion of this discussion by a surgeon. It would be foolhardy to talk to anaesthetists about phenomena which they can better observe for themselves. Nor is there any particular reason why a surgeon should be invited to discuss pharmacology, endocrinology or the physiology of the circulation and respiratory apparatus. But we can still claim the wound as our province whether we make it ourselves or are merely called in to treat it. The province of the surgeon can moreover logically be extended to include what has always been his by tradition, by insisting that all injuries are wounds. As an accident surgeon I am concerned with the diagnosis of the nature and extent of wounds—which brings me to the third reason for the choice of title—my conviction that the main cause of the phenomena under review lies in the wound itself—a wound of the circulation which results in bleeding. In the early stages following injury other than burns, the overriding factor contributing to those states of circulatory disturbance commonly called " shock "—is haemorrhage.

I admit that there are states associated with injury sometimes labelled " shock," that are but indirectly related to local injury ; even that they sometimes arise from treatment administered by surgeon or anaesthetist. They may be due to illness preceding the fall and the trauma. But it is time we got away from any vague use of the word " shock " in a semi-lay sense or even as an umbrella to cover phenomena associated with such differing incidents as pulmonary embolism, coronary thrombosis, cardiac failure, diabetic coma, circulatory collapse following a head injury, anaphylaxis, peritonitis or ether intoxication. Grant and Reeve (1951) discussing observations made during the second world war discouraged the use of the word " shock " at all. They suggest that as a clinical description it should be replaced by detail of signs and symptoms. They endeavoured to put an end to its use as an abstract concept by talking about the *early circulatory changes of the illness of trauma.* They confined their discussion to investigations on man and cleared the ground for recognition (i) that the extent of bleeding following injury has in the past been grossly under-estimated and (ii) that the treatment of moderate

and major injuries requires transfusion of much larger quantities of blood earlier and more rapidly, than had previously been advised or imagined.

I am aware of a vast array of experimental work on shock and of the massive literature in which it has been reviewed, discussed and theorised about. I have been interested in some of the great controversies that have raged in the past ; for example, the major differences in approach between Blalock (1940) on the one hand and Leriche (1934) and Cannon (1923) on the other—not to mention more recent controversial generalisings by Selye (1950) and Laborit (1952). But I prefer to start from the realities of clinical observation and practice although a bit of my own theorising may creep in towards the end.

One further note of introduction—neglected haemorrhage can lead to a multiplicity of changes—haematological, hormonal, biochemical, nervous, toxic, infective and so on—any of which may be associated with what is called " irreversible shock." In practice we are no longer concerned with the nature of the irreversibility of irreversible shock. We have to deal with particular features of real patients whose states of collapse can only be regarded as irreversible when we have failed to reverse them, because our ignorance of the nature, extent and effects of the injury have resulted in treatment being inadequate. A considerable proportion of our failures have simply been that *transfusion* was inadequate. We are concerned with the possibilities of treatment at a stage when reversibility is still present and at this time haemorrhage is the overriding factor in most recently injured patients. The effects are complicated when the responses of the circulatory system are modified or disturbed by the nature and site of the injury, but even so it is still the wound that is decisive.

I shall illustrate what I mean by " wound shock " by reference to individual patients but must first discuss the nature of the evidence that has stimulated and in turn been reinforced by the observations of a team of investigators at the Birmingham Accident Hospital during the last six years.

The key problem is the old one of " where the blood goes to." Direct measurement of blood loss to the outside or into the tissues is almost impossible except in the operating theatre where blood loss can be checked by weighing swabs and measuring the contents of the suction bottle. Even then it is important to note that this does not measure the oozing into dressings and tissues which is so important in many major orthopaedic procedures.

In the absence of direct measurement the basic evidence for the extent of blood loss following injury is derived from blood volume studies. The evidence has existed since World War I (Keith 1919 *a* and *b*). The long continued failure to recognise its implications derives firstly from an emotional incapacity to admit that so much blood could in fact be lost. This attitude has been further coloured by theoretical considerations. Those who thought that " shock " was due to a widespread increase in

capillary permeability were unwilling to accept evidence from plasma volume studies which might be invalidated by plasma leakage. Others were misled by the concept that a reduction in blood volume was simply a reduction of " circulating " blood and that the missing blood was in the capillary bed. The apparent reasonableness of this argument derives in turn from two other considerations ; firstly that in the final stages of " shock," even where haemorrhage has been the decisive cause, the tone of the capillaries is eventually lost, transfusion becomes useless and the patient bleeds to death into his own capillaries. Secondly, there are forms of systemic collapse following injury where capillary dilatation is a primary factor during the early stages. Direct proof of the present thesis is even now less certain than appears at first glance. The main argument is based, however, on three features of the total evidence :

1. That we have never found any evidence of a return to the circulation of the missing red cells supposed to be trapped in the capillary bed, even when all the clinical features of so-called shock have been removed by transfusion.

2. We have much corroborative evidence to suggest that the reduction in blood volume is of the order that would be expected from the amount of bleeding as assessed from a study of the local injuries.

3. The final evidence that makes it necessary for us to reconsider our attitude to earlier theories is the dramatic effect produced by adequate transfusion of stored blood.

Certainly we must now take seriously the results of blood volume studies following injury. There are available a number of new methods in which cells are labelled with the radioactive isotopes P^{32}, Cr^{51}, or the plasma with I^{131} or I^{132}. The accuracy of these methods has been checked in " normals " and in a variety of non-acute conditions. It has been further checked by our team by repetition in the same subject, by carrying out two methods simultaneously and by comparing the results with other haematological and clinical evidence (Davies and Topley, 1959 ; Topley, Davies and Fisher, 1959). The main inaccuracy in using blood volume studies to determine the extent of loss of blood or other fluid from the circulation in trauma is that the pre-accident blood volume is unknown and an error arises from taking an average normal by weight, height or surface area. For practical purposes the patient's height measured on admission is the most useful basis.

In the early stages of our work (Clarke, Topley and Flear, 1955) we concentrated on red cell volume studies carried out after the patient had recovered from the phase of circulatory instability. In the presence of a clinically normal circulation there is no evidence to suggest that such determinations are less accurate twenty-four hours after injury than in the normal. The total error probably amounts to less than 10 per cent. of the blood volume. In severe burns and in patients whose circulations are unstable after major injury, we are still investigating the accuracy

of blood volume studies. All the evidence has shown that civilian injuries resemble battle injuries in the extent of blood loss and the uniformity with which it has previously been under-estimated, particularly in closed injuries with fractures of the limbs and trunk.

Some of this evidence is visual and circumstantial and it is important to establish a visual picture of some basic facts. Our calculations are based on a blood volume chart composited from the evidence available. Taking from this chart the extremes and an intermediate we get an idea of the range of normal blood volumes in pints and litres (Fig. 1).

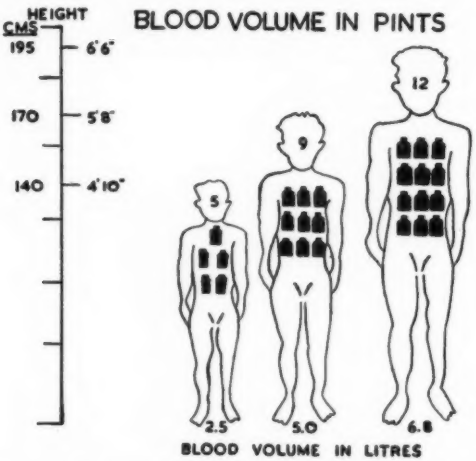


Fig. 1

In discussing transfusion it is to be noted that a bottle of blood contains, in the Birmingham region for instance, 120mls. of anticoagulent fluid and only about 400mls. of whole blood (Fig. 2). In very large transfusions the extra load of fluid and citrate may be important (Hejhal and Firt, 1954; Firt and Hejhal, 1957). In moderate transfusions and with moderate speed of transfusion, we have not found the disposal of this fluid or the dose of citrate to be of major significance. In any case if we now consider our patients of different sizes in terms of numbers of bottles of blood required to replace their total blood volume with whole blood, we see (Fig. 3), that it needs six to seventeen bottles.

Repeated blood volume studies have indicated the extent and timing of blood loss from a variety of injuries. A group of moderately severe fractures of the tibia and fibula either open and requiring surgery or closed and being treated by open operating and plating, showed blood loss on admission ranging from one-half to two litres and averaging about one litre, with a total red cell loss corresponding to a blood loss of one and a half to three and a half litres and averaging about two litres.

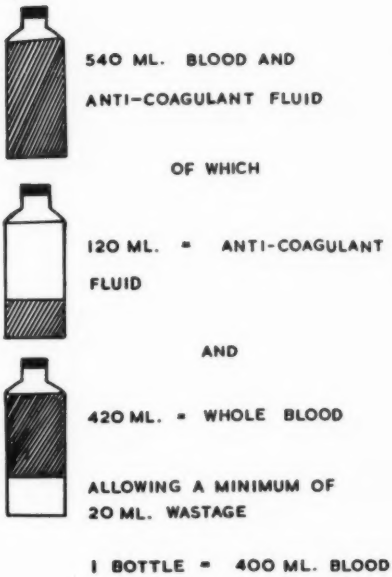

1 BOTTLE OF 'BLOOD'
CONTAINS
540 ML. BLOOD AND
ANTI-COAGULANT FLUID
OF WHICH
120 ML. = ANTI-COAGULANT
FLUID
AND
420 ML. = WHOLE BLOOD
ALLOWING A MINIMUM OF
20 ML. WASTAGE
1 BOTTLE = 400 ML. BLOOD

Fig. 2

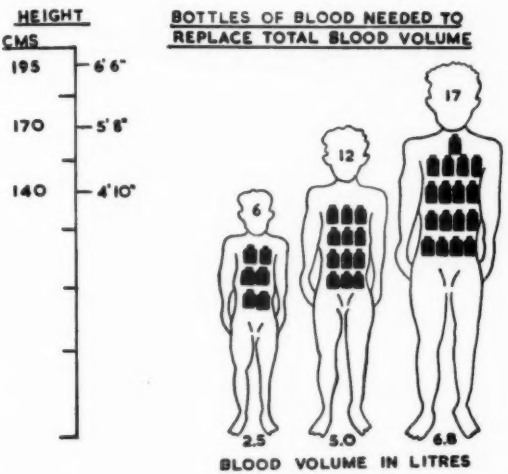

HEIGHT
CMS
195
6'6"
170
5'8"
140
4'10"
BOTTLES OF BLOOD NEEDED TO
REPLACE TOTAL BLOOD VOLUME
6
12
17
2.5
5.0
6.8
BLOOD VOLUME IN LITRES

Fig. 3

Other patients with lower limb injuries showed greater variation with closed fractures of the femur losing anything from one half to two and a half litres without massive swelling, and other moderate open injuries losing one half to one and a half litres during the first few hours and twice that amount over the first few days. Upper limb injuries with moderately severe laceration sometimes involving main arteries frequently revealed a primary blood loss of as much as two litres. Later blood loss was relatively less from wounds where haemorrhage was controlled and damage opening up tissue planes did not permit continued extravasation.

A number of patients with crushing injuries to the chest with unilateral fractured ribs and without major lung complications, showed an average primary blood loss of a little over a litre with total blood loss ranging from two to three and a half litres, largely contributed to by damage to the chest wall. In abdominal injuries we have found blood loss to be extremely variable and difficult to predict. In fractures of the pelvis blood loss has frequently been severe on admission and has continued through the following period of hours and days. Many patients with fractures of the pelvis have lost two to three litres (40 to 50 per cent. of their total blood volume) during the first few hours and as much again or more during the first few days.

A large series of patients with severe multiple injuries showed variable blood loss but with an increasing number of patients who have remained alive following massive primary blood loss and severe haemorrhage into the tissues continuing for several days. In many of these cases the total blood loss has exceeded the normal blood volume by 50 per cent.

At this stage it is important to discuss one objection to our conclusions. It is suggested that our patients only bleed because we transfuse them. Repeated blood volume studies on patients with moderate injuries who for one reason or another escaped transfusion, showed their blood loss to be of the same order as similar patients where replacement transfusion was carried out. Early blood volume determinations before transfusion was started have provided further evidence that the extent of blood loss in moderate and in some quite severe injuries is not due to transfusion. In the most severe injuries transfusion does increase the total blood loss. The alternative is often permanent cessation of bleeding with the onset of irreversible death. Some patients have continued to bleed in spite of surgery and transfusion and presented impossible problems from the point of view of haemostasis. In the majority of the multiple injuries we have investigated, transfusion with their blood volume or more allowed haemorrhage to be brought under control and was followed by recovery.

Now we must return to the problem of where all this blood goes to. Our answer is simple—it is lost by haemorrhage from the wound to the outside and into the tissues. The external bleeding cannot be measured so we have tried to build up a picture of the appearance of different quantities of blood by photographing measured volumes of red current

jelly or bull's blood in clinically relevant situations (Clarke *et al.*, 1956.)

On the other side of the picture—blood loss into the tissues is quantitatively at least as important, often much more so, more difficult to appreciate and more neglected.

Our first assumption is that swelling present within an hour or two of injury is mostly whole blood. Even if this is not completely true at least the volume of swelling represents a space where that much fluid can hide and haemoconcentration is rare. There is moreover some evidence to suggest that in fractures and other deep injuries extravasation of blood is followed by reabsorption of fluid even while the bleeding continues so that there is probably a differential loss of red cells rather than plasma.

Grant and Reeve (1951) classified wounds as small, moderate, large and very large, and correlated this with blood loss and clinical signs. They used the fist as a crude measure of the volume of damaged tissue. In civilian injuries we prefer to think in terms of volumes of bleeding but the fist is a useful crude guide to a pint (half-litre) volume.

Measurement of swelling associated with closed injuries has been done in three ways. Firstly, we measured the difference between a swollen and normal limb by immersion in water up to a known mark and recording the difference in the volume displaced. The method is probably accurate to a fifth of a pint.

Secondly we marked off the limbs every 2cms. and measured the circumference. We then calculated the volume of a series of imaginary cylinders and again checking with controls showed the method to be accurate enough for our purpose.

Having taken quite a lot of trouble with such measurements we tried to find a simpler method of identifying volumes of swelling and this led to our third technique with pieces of felt. Volumes of surgical felt can be measured to represent different volumes of swelling and then applied to the limbs or trunk to imitate the effects of clinical lesions. The experiment is readily repeatable. (Clarke *et al.*, 1956.)

Consideration of the volume of blood that can be extravasated at the site of closed injuries goes a long way to answer the question of where the missing blood can get to. To this evidence must be added the logical deduction that a fractured pelvis can lose much more than the swellings we have been looking at and that a thigh with a fractured femur can sometimes contain something like a gallon. Is it then surprising that fractures of the femur suddenly collapse in transportation?

Case 1. A young man was involved in a road accident and admitted pale, cold; blood pressure 110/80, pulse rate 100. Within the next half hour the blood pressure had fallen to 90/40, the pulse had risen to 130. The injury included a compound fracture of the shaft of the femur, dislocated knee and a wound of the foot. With ten bottles of blood the femur was nailed and the wound sutured. There was a time back in the ward when he did not look quite so good but finally he made an excellent recovery. Blood volume studies indicated that by the time he had finished oozing into his wounds he was still five bottles of red cells down.

Case 2. Another patient sustained a wound of the forearm which divided radial and ulnar arteries. A local doctor had applied a pressure bandage. On admission to hospital he was pale, cold, pulseless, with practically no blood pressure. He responded rapidly to transfusion, suture of the ulnar artery and ligature of the radial artery. He received a transfusion of eight bottles.

Case 3. A young boy was involved in a road accident sustaining a fractured olecranon, bruised thigh, fractured patella and a severe open fracture of the tibia and fibula. On arrival at hospital the dressings and his trousers were soaked with blood. His blood pressure was 135/75 falling to 110/60, pulse rate 135; pale and cold. With transfusion the wound was explored; no major vessels have been divided. He received a transfusion of nine bottles of blood in spite of which his haemoglobin fell to 12.9gms. per cent.

Case 4. The next patient was run over. He presented a rather different picture —pallor certainly, anxiety very much so, blood pressure 120/90, pulse rate 110. The blood pressure rose to 180/126 and the pulse rate increased to 140 before transfusion was begun. He received five bottles of blood during the course of resuscitation and four more by the end of the amputation. Blood volume studies suggested that he was missing the red cell equivalent of three bottles of blood by the second post-operative day.

Case 5. A young lad also involved in a road accident who reached hospital three hours after injury, pale, cold, pulse feeble, 120 per minute, blood pressure 80/56. He had major fractures of the right femur, left humerus and tibia and fibula, multiple bruises and abrasions. As his general condition improved with transfusion he developed abdominal signs and was found to have lost nearly a litre of blood from a ruptured spleen. He received a transfusion considerably greater than his total blood volume and made an excellent recovery.

Other patients do not require blood with the same degree of urgency but transfusion can make definitive surgery possible with the minimum of risk

Case 6. A forty-year-old man sliced off his hand in a chocolate machine. On admission blood pressure was 150/90, pulse rate 80. The wound was closed by an abdominal flap. A major wound of the elbow required an additional skin graft. He was given three pints of blood in spite of which his haemoglobin was 12.9 gms. per cent. on the eighth day.

Having discussed some individual patients and got some idea of the sort of transfusion we have given to moderate injuries we can now consider the relation between systemic physical signs of so-called " shock " and blood volume levels. Earlier observations by Grant and Reeve (1951) have been repeated for civilian injuries by Fisher (1958). A low total blood volume was associated with a low blood pressure. A blood pressure higher than normal was associated with a blood volume not less than 75 per cent. of normal. But a normal blood pressure may be associated with a blood volume reduced to 80, 70 and even 60 per cent. of normal. The only patients with slow pulse rates had normal blood volumes. Most of those with raised pulse rates had low blood volumes. But many patients with blood volumes reduced by 20 to 40 per cent. had normal pulse rates. Even when the total blood *volume* has been returned to 80 per cent. of normal by haemodilution or plasma transfusion, a raised pulse rate may still indicate a lowered red cell volume. As for the other signs, both cold and warm extremities were associated with red cell

volumes greatly reduced by haemorrhage. In the same patients the veins were constricted or relaxed. It is only when we consider the presence or absence of skin pallor that there is any real difference. The majority of patients with low blood volumes are pale although here too it is important to note that patients whose red cell volumes were reduced to 55 to 75 per cent. of normal as a result of haemorrhage could still be pink !

So far we have considered these signs in relation to blood volume in a somewhat static way. There is no time to pursue the full extent of the changes that can occur (i) with time and spontaneous haemodilution or further bleeding ; (ii) with transfusion, and (iii) with anaesthesia, surgery and recovery from both. It is important to realise that whilst on the one hand haemodilution is tending to return the plasma and total blood volume to normal, on the other hand many injuries continue to bleed for hours and days.

In addition we are often faced with a situation in which we are no longer concerned with the extent of diminution of total blood volume or red cell volume---but with the question of when to stop or slow transfusion, of the signs and symptoms which indicate the restoration of a normal blood volume. The blood pressure may return to normal and the pulse rate start to fall long before this has been achieved. The patient becomes warm and pink and anaesthesia alone may facilitate this is a misleading way. I have been impressed with the fact that the toes become warm and pink last of all and that this is frequently a valuable indication of the fact that the total blood volume is nearly normal. We have recently been concerned with the evaluation of the state of visibility and filling of neck veins as an indication of adequate transfusion. Under some conditions it is possible for venous congestion to develop in the presence of cold extremities, vasoconstriction and a low blood volume. On the other hand when everything points to the absence of persistent vasoconstriction, the appearance of the veins may indicate that the circulation has been filled. Further observations are required for clinical signs can be of very great value and are not displaced by our radioactive isotope cunning. On the other hand there are times when all blood loss has apparently been covered by transfusion yet the patient still looks as though haemorrhage may be continuing. Increasingly we are finding occasions when a determination of blood volume can give a valuable clinical guide to assessment and treatment.

One thing emerges clearly—a patient with a normal blood pressure, normal pulse rate, pink, warm and with good arm veins, may have already lost 30 to 40 per cent. of his total blood volume by bleeding within the hour. Yet severe collapse with low blood pressure, rapid pulse, extreme pallor or a grey colour, cold extremities and sweating, usually indicates a blood loss of at least 50 per cent. When signs of collapse are not present the nature and extent of injury is a better guide to what is likely to happen

than any considerations derived from external evidence of the state of the circulation.

So far we have summarised evidence of the extent of blood loss and its significance as the major factor underlying circulatory disturbances following injury. There is much more to be said in this context alone and I have no space to do more than summarise some clinical consequences. From the point of view of treatment, transfusion of whole blood is of decisive importance in the treatment of established shock following injury, whether the bleeding be obvious or concealed. In addition whole blood transfusion is invaluable in the *prevention* of states of circulatory collapse. In fit individuals there can be no question that a pint or two of blood loss can be tolerated without appreciable risk, but even this amount of bleeding may be significant when further bleeding is expected or when major surgery and anaesthesia are necessary. In patients who are sick or old or when the injuries themselves predispose to infection or systemic sequelae, even the loss of one to two pints of blood may be decisive. This is particularly so in children and small adults where it constitutes a higher proportion of total blood volume than it does in the big and muscular. Transfusion permits adequate primary surgery. It plays a part in the prevention of wound infection and helps to modify the complex metabolic and other disturbances which comprise the " illness of trauma."

A full appreciation of the role of transfusion requires some consideration of the processes or adaptation of the circulation to blood loss. The failure of the blood pressure and pulse rate quantitatively to reflect a fall in blood volume can easily be explained. Recent experimental observations in man have shown that blood can be transferred from the pulmonary to the systemic circulation following haemorrhage to the extent of about three-quarters of a litre. (Henry 1955). Further bleeding can be compensated for by decrease in the volume of blood contained in the liver, spleen and portal circulation generally. Other adaptive mechanisms allow progressive loss to take place without a fall in blood pressure, but sooner or later this becomes evident in the form of skin pallor. Beyond a certain level the maintenance of a normal blood pressure is only made possible by a decreased blood flow to essential organs including the kidney and liver. At some time during the course of bleeding or as a result of associated stimuli, the pattern of response may be altered and the blood pressure falls. This can occur in the presence of continuing vasoconstriction but can also occur suddenly and take the form of the vaso-vagal attack with opening up of blood flow through muscle. Such " neurogenic shock " involving a complete change in the pattern of nervous control of vascular tone throughout the body may sometimes be an important defence mechanism by dropping the blood pressure and facilitating clotting and control of bleeding from damaged vessels. Provided that this state of affairs continues only for a short period, possibly up to as much as half-

an-hour or longer, it may be beneficial. Active treatment may be inadvisable apart from the removal of the cause by transfusion and surgery for the control of bleeding. The difficulty in diagnosis arises because the same sudden response which may occur beneficially in the presence of acute bleeding, may also be fired off by a variety of stimuli in the absence of any bleeding at all. When the fall of blood pressure is maintained in spite of continued vasoconstriction serious damage to important organs is probable.

Occasionally after bleeding and adequate transfusion hypotension may result from a failure of the circulation to regain vascular tone so that it is desirable to consider the use of vaso-pressor drugs. Usually it is likely to do harm and I have not yet seen a patient for whom Noradrenaline was indicated. The drug is certainly effective as evidenced by the skin sloughing that has followed its use.

The question of other drugs that can modify the circulatory response from morphia and pethidine to largactil and its successors is more complex. We are frequently faced with disturbances of the response to bleeding, sometimes associated with overt anxiety, sometimes with hypertension and vasoconstriction affecting both arteries and veins, which are harmful and which may even prevent the restoration of a normal blood volume. Such complications are most common in the presence of injury affecting the pulmonary circulation, and it is certainly no use aiming to restore a blood volume unless the circulation can continue through both systemic and pulmonary circuits. The use of such drugs in association with transfusion is still basically empirical. We are engaged in studies of cardiac output, central venous pressure and the application of a variety of physiological techniques to the evaluation of the severely injured patient. Suffice it to say that for the time being I consider the use of these drugs as ancillary to transfusion and that early restoration of a normal blood volume provides the best opportunity to deal with other phenomena amenable to treatment. In the presence of a low blood volume attempts to maintain the blood pressure by means other than transfusion are likely to be ephemeral. The fact that the reactions of the organism are changed completely by general anaesthesia, quite apart from the particular effects of particular drugs is recognised by my anaesthetic colleagues. There is much room for further investigation of the significance of circulatory signs in relationship to blood volume under anaesthesia in general and with specific forms in particular.

In conclusion I would repeat that until we are aware of the extent of blood loss and have attempted its early adequate replacement, we are not in a position to sort out the contribution of other factors to any syndrome of so-called shock. As our information increases I think we will replace any need for a general concept of shock by more accurate physiological knowledge of particular conditions. Meanwhile the extent of blood loss and the value of its replacement requires to be appreciated much more

widely, and this appreciation is useless unless it is associated with the facilities necessary for adequate diagnosis, surgery and transfusion.

REFERENCES

BLALOCK, A. (1940) *Principles of surgical care.* C. V. Mosby, St. Louis, and Henry Kimpton, London.

CANNON, W. B. (1923) *Traumatic shock.* Appleton, New York.

CLARKE, R. (1956) *Brit. J. clin. Pract.* **10**, 739.

——————— TOPLEY, E., and FLEAR, C. T. G. (1955) *Lancet* **1**, 629.

DAVIES, J. W. D., and TOPLEY, E. (1959) *The critical evaluation of red cell and plasma volume techniques in patients with acute injuries.* (To be published).

FIRT, F., and HEJHAL, L. (1957) *Lancet* **2**, 1132.

FISHER, M. R. (1958) *Clin. Sci.* **17**, 181.

GRANT, R. T., and REEVE, E. B. (1951) *Spec. Rep. Ser. med. Res. Coun., London.* **277**.

HEJHAL, J., and FIRT, F. (1954) *Otázky lečení prudkého kruácení.* Nakladatelsvi Ceskolvenské Academie Vêd, Praha.

HENRY, J. P. (1955) Orthostasis and the kidney. *Wright Air Development Centre, Technical Report* 55-478. United States Air Force, Ohio.

KEITH, N. M. (1919a) *Spec. Rep. Ser. med. Res. Comm., London, No.* **26**, Section VIII.

——————— (1919b) *Ibid., No.* **27**.

LABORIT, H. (1952) *Reaction organique à l'agression et choc.* Masson, Paris.

LERICHE, R. (1934) *Lyon chir.* **31**, 627.

SELYE, H. (1950) *The physiology and pathology of exposure to stress.* Montreal.

TOPLEY, E., DAVIES, J. W. D., and FISHER, M. R. (1959) *The clinical consistency of red cell volume studies following injury.* (To be published).

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A NOTE ON THE SEMIMEMBRANOSUS MUSCLE

by

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CERTAIN CONSTANT FEATURES of the attachments of M.semimembranosus escape notice in the generality of formal descriptive accounts of this muscle. In British text-books the muscle origin is confined to the superolateral " facet " on the ischial tuberosity. Regarding the insertion, emphasis is upon the attachment to the " groove for semimembranosus " on the medial tibial condyle, concomitant attachments being treated as secondary expansions and an essential one being completely ignored. For this incompleteness of treatment Thane (1892) may be primarily responsible, since the authoritative 10th edition of *Quain* may have influenced all subsequent anatomical treatises. The French anatomists, notably Poirier and Charpy (1901), give the semimembranosus insertion at least a descriptive consideration more in accord with nature.

The proximal and distal attachments of the semimembranosus were studied in twenty-one dissecting room subjects and the results of this exercise are presented briefly herein. They emphasize (1) the presence of a secondary but constant origin of the muscle; (2) the functional importance of the constant but commonly ignored vertical deep tendinous slip of insertion to a *tuberculum quadratum tendinis* of the tibia.

Origin of the muscle

On the tuber ischii the conventional areas of origin of (*a*) M.semimembranosus and (*b*) the conjoint Mm.semitendinosus et biceps femoris are separated by an obtrusive linear elevation (Fig. 1*a*, x). This is generally regarded, by implication, as representing a demarcation between two contiguous areas of origin, but, in fact, results from the direct attachment of tendinous fibres of origin (Figs. 1*b*, 1*c*) including fibres of M.semimembranosus.

Attempted separation of the tendon of origin of M.semimembranosus from the conjoint tendon of origin of Mm.semitendinosus et biceps is resisted by three groups of connectant collagenous fibres. Of these the first, described by Weber and Collin (1904), is a sheet-like condensation, whose fibres arch transversely and superficially over the two tendons and gain attachment to the medial and lateral borders of the ischial tuberosity.

The second is " un tissu dense dans lequel on trouve quelquefois une bourse séreuse " (Poirier and Charpy) found by Weber and Collin in the majority of their specimens. Its fibres arise from the deep aspect of either, or of both, of the components of the biceps-semitendinosus tendon and are inserted into the superficial aspect of the semimembranosus tendon. The third group comes into view after division of the first and second groups, and comprises fibres of origin of both the semimembranosus and the conjoint hamstring tendons. These fibres fan out beyond the con-

ventional tuberal areas of origin to become mutually interwoven in successive layers at and beyond their respective sides of the oblique tuberal line (Fig. 1*b*). In this region, therefore, the semimembranosus tendon and the common hamstring tendon are inextricably conjoined and each has a strong attachment to the oblique line.

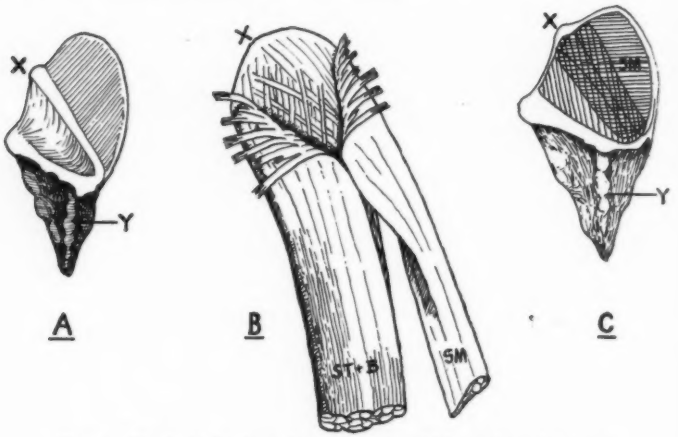

Fig. 1. The ischial tuberosity and origin of M. semimembranosus.

The primary origin of the M.semimembranosus is thus from the supero-lateral "facet" of the ischial tuberosity and from the tuberal oblique line. It is reinforced by a secondary origin in the form of a falciform tendinous expansion, some inch to inch-and-a-half long. This takes a linear origin from the roughened lateral border of the tuberosity and from the adjacent perineal border of the ischial ramus and is here situate behind M.quadratus femoris and in front of M.adductor magnus (see Fig. 2): the fibres of this falciform expansion (which resembles somewhat an open razor) spread down into the whole extent of the principal semimembranosus tendon, which becomes flattened below its origin.

By virtue of this dual origin, M.semimembranosus has a firm hold upon the ischial tuberosity, which it grasps somewhat in the fashion of the fingers and thumb of a Pawlik's grip.

From the medial margin of the principal semimembranosus tendon a fibrous expansion passes deep to M.adductor magnus to gain attachment to the vertical ridge (Fig. 1*a*, y) on the lower part of the posterior surface of the ischial tuberosity and to the contiguous deep edge of the perineal border of the ischial ramus (see Fig. 2). Occasionally an additional fibrous expansion is present, of similar origin, but becoming continuous with M.adductor magnus.

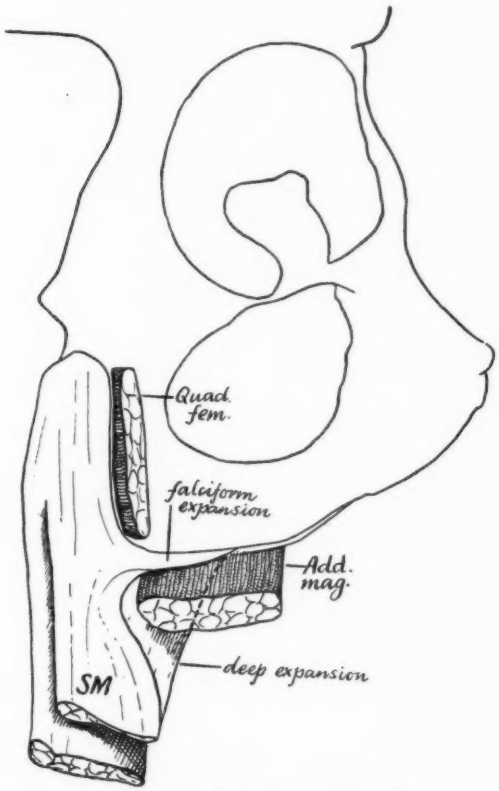

Fig. 2. Origin of M. semimembranosus.

Insertion of the muscle

No descriptively adequate account of the semimembranosus insertion appears in British anatomical treatises and a substantial tendinous slip of functional importance is completely ignored. Perhaps the nearest approach to realism is that of Frazer (1920) from meticulous osteological observation. The French anatomists' accounts of this insertion are superior in substance and emphasis, Poirier and Charpy (1901) recognizing the division of the main tendon of insertion into " tendons direct, récurrent et réfléchi " and Testut (1904) noting " trois faisceaux divergents, descendant, récurrent et antérieur."

As dissection reveals, the inferior tendon of M.semimembranosus subdivides at about knee-joint level into four distinct and recognizable components. In order of importance these are :

1. A short, stout, strong tendinous slip (Fig. 3*a*, x), descending from the line of the main insertion tendon and firmly attached to a prominent, squarish tubercle (*tuberculum quadratum tendinis*) on the postero-lateral

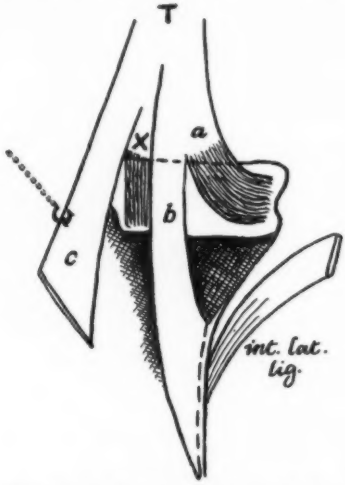

Fig. 3*a*. Insertion of M. semimembranosus (diagrammatic).

aspect of the medial tibial condyle (Fig. 3*b*, x). Poirier and Charpy, and likewise Testut, take notice of fibres attached here, derived from their "direct" or "descending" slip of insertion, but recognize neither a

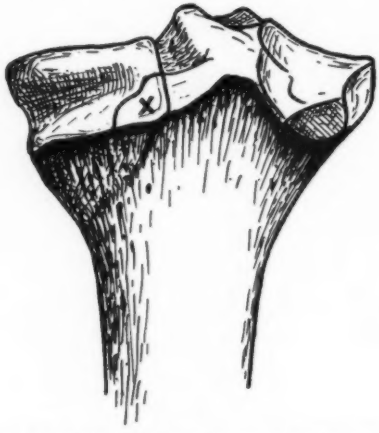

Fig. 3*b*. Head of tibia, showing tuberculum quadratum tendinis.

special tubercle (so evident on inspection) nor the functional importance of the " direct " slip.

2. An expanded, thin superficial tendon (Figs. 3*a* and 4), obscuring the deeply lying first component and proceeding infero-medially to an insertion upon the medial margin of the tibia immediately behind the medial ligament of the knee-joint, and commonly descending beyond the lower end of that ligament. This component takes the form of a sheaf of discrete, imbricated slips (Fig. 4*b*), which cross the medial inferior genicular vessels in their soft fatty bed and curve somewhat forwards to the tibial

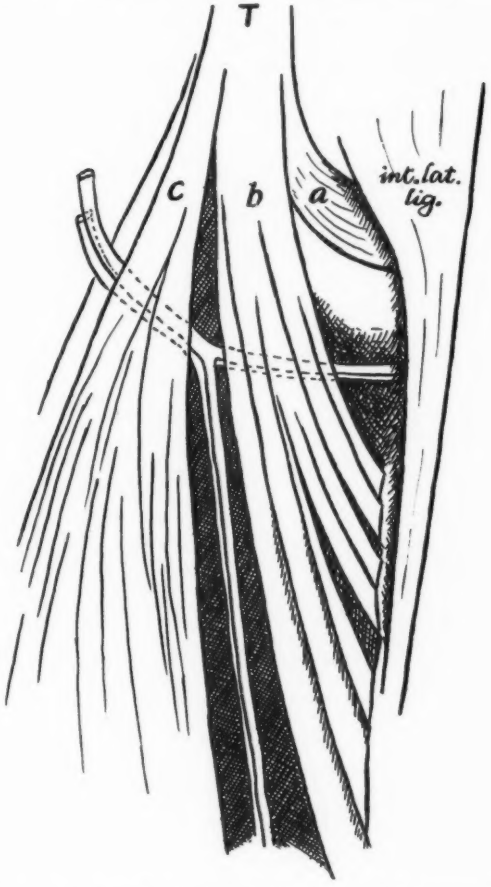

Fig. 4. Insertion of M. semimembranosus (semi-diagrammatic).

margin. Thereon they produce a distinct linear asperity, which in well-marked bones has the form of a discontinuous series of minute tubercles. The insertion of the imbricated slips, although contiguously deep to, is wholly independent of, the posterior free margin of the medial (internal lateral) ligament of the knee-joint. A substantial descending branch from the medial inferior genicular artery follows the posterior border of this sheaf-like component (Fig. 4).

3. A thin aponeurotic expansion covering M.popliteus and gaining an indirect attachment to the soleal (popliteal) line (Fig. 4, *c*).

4. A thick, funicular, recurrent tendon passing infero-anteriorly, deep to the medial ligament of the knee-joint, to gain attachment to the inferior lip and neighbourhood of the " groove for semimembranosus " on the medial tibial condyle (Fig. 4, *a*). This is the component commonly emphasized.

5. A variable number of irregularly disposed fasciculi, collectively constituting the oblique popliteal ligament (lig.posticum Winslowi) and arising from the deep aspect of the main tendon of insertion. This component requires no present detailed description.

These several subdivisions of the main tendon of insertion of M.semimembranosus are barely separate in the well-developed subject, being but parts of a single expanded tendon in the form of a flattened demi-cone, having deep and superficial parts. The fibres attached to the soleal line and to the tibial medial border are, in the early stages of tibial flexion, in the direct line of pull of M.semimembranosus : in the later stages they are doubled back upon the parent tendon. When upward traction is exerted upon the cadaveric muscle they are seen to be more tense early in flexion and to become much less so as flexion proceeds. The fibres of the recurrent slip to the horizontal groove are, on the contrary, in the direct line of muscle pull only when genuflexion has attained an amplitude of 90degs. At the beginning of flexion their direction is at a right angle to that of the parent tendon. When upward traction is exerted upon the muscle they are seen to be most tense in the later stages of flexion and least so in the earlier stages.

The strong central slip to the tuberculum quadratum tendinis remains constantly in the direct line of muscle pull and is equally taut in all stages of genuflexion. Hence it must be recognized as being functionally the main attachment of M.semimembranosus to the tibia.

REFERENCES

FRAZER, J. E. (1920) *Anatomy of the human skeleton*. 2nd edit. London, Churchill.
POIRIER, P., and CHARPY, A. (1901) *Traite d'anatomie humaine* **2** (1), 238-241. Paris, Masson.
TESTUT, L. (1904) *Traité d'anatomie humaine* **1**, 964-965. Paris, Doin.
THANE, G. D. (1892) *Quain's Elements of Anatomy* 10th edit. **2** (2), 251. London, Longmans.
WEBER, A., and COLLIN, R. (1904) *Bibliog. anat. Paris* **13** (3), 149-160.

THE CENTENARY OF THE RE-INTERMENT OF JOHN HUNTER

by

Sir Gordon Gordon-Taylor, K.B.E., C.B., M.A., F.R.C.S.

A CENTENARY OCCASION suggests some form of commemoration or celebration: this note is merely a recording of facts. Preparation for an address in the Church of St. Martin-in-the-Fields on the occasion of the unveiling and dedication of a plaque to John Hunter on 14th February 1952 made the writer aware that after the lapse of another seven years a century would have passed since Hunter's remains were removed from St. Martin-in-the-Fields, where they had lain from 22nd October 1793 till 26th March 1859, to Westminster Abbey, where they were re-interred on 28th March 1859.

The word "exhumation" possesses a ghoulish sound, whether performed as part of the orderly investigation of some suspected crime or a century ago as a source of ill-gotten gain for those who furnished the anatomical schools and the surgeons themselves with human material for dissection. The archaeologist's exhumation and spoliation seem less distasteful to the scientific mind, especially since the efforts of the searchers are directed less to the remains of some prehistoric hero than to the ornaments, rings, vases, bracelets, figurines and other trinkets that were considered the proper *apanage* of the "captains and the kings" who had left this life. Even Sir Thomas Browne in the Epistle Dedicatory to Hydriotaphia writes: "Who knows the fate of his bones, or how often he is to be buried."

Hunter suffered a "disentombment," but this only resulted from an Order in Council to the effect that the coffins deposited in any of the vaults under St. Martin's Church or in any of the catacombs under the churchyard could be removed by relatives or else they would be re-interred in the vaults or catacombs which would be finally closed. The story of Frank Buckland's search in the Crypt and the ultimate finding of Hunter's coffin has been told before in the pages of *The Annals*. Much is owing to Buckland for his great enthusiasm over Hunter's work and repute which induced him to embark upon the strenuous task in St. Martin's, for the fortunate *soupçon* that sent him to the appropriate office to ascertain with certainty that Hunter was in fact "buried" in St. Martin's, for the interest that he aroused in the College Council by reason of the discovery of Hunter's coffin, by his recollection of how anxious was his own father, formerly Dean of Westminster, that a bust of Hunter should be placed in the Abbey, by his own personal and successful approach to several members of the Chapter along with "propositions" of the Council: and indirectly through the stir caused by the discovery of Hunter's coffin by the formation of a committee to raise funds for erecting a statue of John Hunter. The powerful committee appointed did include Buckland: and John F. South,

one of the Vice-Presidents of the College, was Honorary Secretary of the Committee: the Committee first met on Tuesday 29th March the day after the Abbey ceremony. A sum of £1,172 17s. 1d. was collected and Weekes was selected to make the statue, a reproduction in marble of the well-known Reynold's portrait of Hunter in the Council Room.

The Invitations to the ceremony in the Abbey were sent out by the Royal College of Surgeons of England (Fig. 1): some 600 people attended.

Reinterment of the Remains of
JOHN HUNTER
IN
Westminster Abbey
on Monday, the 28th instant, at 1 o'clock P.M.
Admit Mr
To the Jerusalem Chamber through Poet's Court
No Admission after Seven o'clock
No 584
Edm Belfour Secy

Fig. 1

It had been anticipated that the President of the College, J. H. Green, would deliver an address, but this was not given. Among the distinguished surgeons and scientists who attended were the Dean of Westminster, Dr. Stanley; Professor (later Sir) Richard Owen; representatives of the Royal Colleges, the Society of Apothecaries, the Linnaean Society, the Royal Medico-Chirurgical Society, the Medical Society of London, the Hunterian Trustees, and representatives from the London hospitals, including Messrs. Stanley of St. Bartholomew's, Solly of St. Thomas's, Hancock of Charing Cross, Temple Frere and Alexander Shaw of "Middlesex," Tatum of St. George's, Holt of Westminster, Gay of the Great Northern, Spencer Smith of St. Mary's, and Sir William Fergusson of King's.

Hunter was buried on the North side of the Nave between Sir David Wilkie and Ben Jonson. Frank Buckland takes special pains to refute the story that at the obsequies the skull of Ben Jonson was "freely handed about": he also makes a statement regarding the coffin while still in St. Martin-in-the-Fields: "I beg publicly to state that the sacred remains of our illustrious founder were in no way meddled with or disturbed by

any person whatever. I feel it my duty to place this on record with my own hand, and on my sole responsibility."

The Leeds School of Medicine, as early at 29th August 1859, presented Frank Buckland with a handsome silver medal commemorating his labours: the Royal College of Surgeons, it is true, on 10th March 1859 forwarded a copy of a resolution of thanks for "active and efficient services in identifying the body of John Hunter." But it was not till 19th December 1864 that Buckland received anything more than this purely formal acknowledgment of "his services"—a copy of the catalogues of the Museum. Buckland acknowledged the gift and spoke of "extreme gratification for the high honour" in being presented with this. Some men are easily satisfied! Or was he laughing at them?

REFERENCES

BUCKLAND, F. (1878) *Curiosities of natural history*. Fourth series. pp. 215 *et seq.*
The Times March 29th 1859.
Annals of the Royal College of Surgeons of England (1952) **10**, 257.

COLLEGE PUBLICATIONS

READERS ARE REMINDED that the following publications issued or sponsored by the College may be obtained from the Editorial Secretary, Royal College of Surgeons of England, Lincoln's Inn Fields, London, W.C.2.

Lives of the Fellows, 1930-1951. By the late Sir D'Arcy Power, K.B.E., F.R.C.S., Honorary Librarian, and continued by W. R. Le Fanu, M.A., Librarian. A single volume, bound in blue cloth, of 889 pages, containing the Lives of all Fellows known to have died between 1930 and 1951. £2 2s. 0d. post free.

A Record of the Years from 1901 *to* 1950. Edited by Sir Ernest Finch, M.D., M.S., F.R.C.S. A slim volume, illustrated, containing a brief history of the College between the centenary and the 150th anniversary of the foundation with Lives of all the Presidents since 1900, written by special contributors from their personal knowledge. In red cloth 9s. post free or red paper covers 5s. 6d. post free.

John Hunter, a List of his Books. A short-title bibliography of all known editions of John Hunter's books, compiled by the Librarian. Printed at the Cambridge University Press, and bound in green cloth. 2s. 6d. post free.

A Guide to the Hunterian Museum (*Physiological Series*). This gives a brief account of the physiological section of John Hunter's museum, the scope, design and historical value of which is unique. 48 pp. 1s.

A Descriptive and Historical Catalogue of the Darwin Memorial at Down House. Charles Darwin and his family lived at Down House, near Orpington, Kent, for forty-two years and it was here that most of his scientific investigations were made, including his work on the Origin of Species, published in 1859. 33 pp. 1s.

The Portraiture of William Harvey. The Thomas Vicary Lecture for 1948 by Geoffrey Keynes, M.A., M.D., F.R.C.S. With a descriptive catalogue and 33 reproductions of the portraits. £1 5s. 0d.

**William Clift*. By Jessie Dobson, B.A., M.Sc., Anatomy Curator. A new biography, fully illustrated, of the first Conservator of the Museum at the College. Published by William Heinemann Medical Books Ltd. Bound in blue cloth; 144 pages with frontispiece portrait and 31 plates. 8s. 6d. post free.

**A separate cheque for this publication would be appreciated.*

ADMISSION TO THE HONORARY FELLOWSHIP

AT THE MEETING of Council on 12th February the Honorary Fellowship was conferred on Dame Lillian Penson, Professor Adams McConnell and Dr. Richard Lewisohn.

In presenting Dame Lillian Penson, Sir Reginald Watson-Jones spoke of her remarkable career in the field of higher education, both in London and in the Colonies. Her contributions to postgraduate medical education had been outstanding and the College owed more to her than it could ever repay for the part she had played in the establishment of the Institute of Basic Medical Sciences. Sir Reginald praised her excellence in the two surgical arts of incision and excision ; the former being evidenced by her swiftness

Fig. 1. Dame Lillian Penson receiving the diploma of Honorary Fellowship from the President, with Mr. A. Dickson Wright, Vice-President, watching.

and clarity of incisive thought and the latter by her ability to eradicate superfluous matter and go direct to the heart of any question under discussion. She was in the truest sense a " noble surgeon," as described by Mallory.

In reply Dame Lillian spoke of the gratification which this wholly unexpected honour had brought to her, and of her delight at being associated with the College which she admired and had been proud to work for. Her satisfaction was, she said, the greater in that she was receiving this honour at the hands of Sir James Paterson Ross.

Mr. Dickson Wright presented Professor Adams McConnell of Dublin

as an outstanding neurosurgeon and teacher who had found new ways of penetrating the skulls of his pupils as well as his patients. Many surgeons in this country had benefited from the warmth of his hospitality and that of his charming wife, whom the Council were delighted to see.

Fig. 2. The President welcoming Professor Adams McConnell to the Honorary Fellowship, with Mr. A. Dickson Wright, Vice-President, listening.

Professor McConnell replied that as a golfer he had always observed the rule " Never hurry your putt—it might be given to you." It was very many years now since he had played his approach shot to the Fellowship by passing the Primary. Now, after some forty years, he had been " given his putt " and he was very grateful. He asked the Council to forgive him if he now basked rather blatantly in his new glory—it was a fine opportunity for him to show his wife what sort of a man it was that she had married.

Sir Gordon Gordon-Taylor introduced Dr. Richard Lewisohn as a distinguished surgeon who had served under eminent teachers on the Continent and had emigrated early in this century to the United States of America. Here he had played a great part in the development of the Mt. Sinai Hospital, New York. Dr. Lewisohn's chief contribution was in the field of blood transfusion, in which his early work had been of fundamental importance. He was indeed entitled to be counted amongst the great benefactors of mankind for this work. He was essentially a modest

man but it could be said of him, to paraphrase the words of Sir Winston Churchill, that " seldom in the field of human endeavour has so much been owed by so many to one man."

Fig. 3. Dr. Richard Lewisohn replying to the citation delivered by Sir Gordon Gordon-Taylor, after receiving the diploma of Honorary Fellowship from the President.

Dr. Lewisohn, in acknowleding with deep gratitude the honour done to him in his declining years, said how proud he was to be the subject of an oration as eloquent and flattering as that delivered by his friend Sir Gordon Gordon-Taylor. He asked leave of the Council to tell them a little of the early history of his work and that of others on blood transfusion. What he had done himself was not in the least complicated or revolutionary and the use of citrate to preserve blood and prevent clotting was already practised when sending specimens to the pathological department. He had merely shown that, when used in the right concentration, the citrate was not toxic, and could therefore be used for blood transfusions. The Russian surgeon Yudin—also an Honorary Fellow of the College—had made use of cadaver blood but this practice was unlikely to find favour in the Western Hemisphere. It was Laudsteiner who had made the greatest contribution by his analysis of the blood groups.

ANATOMICAL MUSEUM

THE SPECIAL DISPLAY for the month of April consists of specimens illustrating different methods of locomotion.

THE HUNTERIAN FESTIVAL

THE HUNTERIAN FESTIVAL was held this year on 16th February, as John Hunter's birthday (14th February) happened to fall on a Saturday.

The proceedings opened with the Hunterian Oration at 4 o'clock by Sir Reginald Watson-Jones, who took as his subject " Surgery is destined to the practice of Medicine." This will be reported in a future issue of the *Annals*.

Fig. 1. The President talking to Sir Reginald Watson-Jones, who had just delivered the Hunterian Oration, with Sir Hugh Lett, Bt., in the background.

The Hunterian Dinner was held in the Great Hall in the evening, with the President, Sir James Paterson Ross, K.C.V.O., in the Chair.

After the loyal toasts and the customary silent tribute to the memory of John Hunter, the Rt. Hon. Sir David Eccles, K.C.V.O., M.P., President of the Board of Trade, proposed the health of the College. Having been born in Harley Street (he is the son of the late W. McAdam Eccles, former Member of Council) and having married a wife from Wimpole Street, he owed a great debt to surgery and had been accustomed to hearing the praises of John Hunter from his earliest days. Life at 124 Harley Street had been devoted to religion and surgery, and surgery meant " Barts " and this College. Sir David told of his father's disregard of money (probably on religious grounds) and his independence of thought : he had disliked the thought of the National Health Service, maintaining that salaried doctors would become trade union minded, but he would have been consoled by the ever-widening influence of the Royal College of Surgeons. The College, like the House of Commons, was an institution which would always have a beneficent influence on those associated with it.

He was proud to be the son of a surgeon and grateful for this opportunity of saying so.

The President, replying, thanked Sir David Eccles for his tributes both to the College and to his father. He spoke of the Hunterian Festival as an opportunity to take stock of the College in the world of medicine and the world itself, and he referred to the history of the College now being written by Sir Zachary Cope. Maturity in an institution, he said, produced confident and easy relations with others, and this was borne out by the presence of so many distinguished people at the dinner. He mentioned the co-operation between the College and the University of London, the maintenance of surgical standards by the Court of Examiners, the continued expansion of the College and its increasing reliance on its officers, many of whom also held important positions elsewhere. Surgery might be losing its importance in some fields, but there was still much relief to give from such misfortunes as accidents and malformations, and still much need for further advances through the Hunterian method of discovery via experiment.

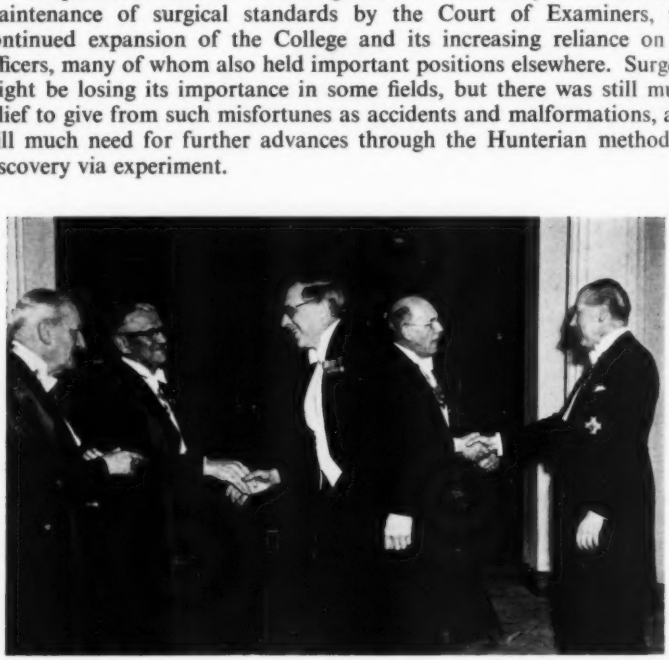

Fig. 2. The President and Vice-Presidents welcoming the Chancellor of the Exchequer and the President of the Board of Trade to the Hunterian Festival Dinner. Left to right: Mr. A. Dickson Wright, Vice-President; Sir Archibald McIndoe, Vice-President; Mr. Heathcoat Amory, Chancellor of the Exchequer; Professor Sir James Paterson Ross, President; and Sir David Eccles, President of the Board of Trade.

The President gratefully acknowledged the help given by his Vice-Presidents and the Council and by the experts from outside the College in such matters as investments and catering. In particular he thanked those conducting the College's Appeal, Lord Kindersley and many others, and all the generous donors who had already come forward with help.

He instanced the Edward Lumley Hall and the Vandervell Chair of Pharmacology, and had a special word of gratitude to Sir Simon Marks for his material help and his boundless enthusiasm and encouragement.

The health of the Guests was proposed by Mr. A. Dickson Wright (Vice-President) who welcomed the many distinguished visitors from the fields of Politics, the Bar, Medicine, Art, and the City, with a last and special word for the Church, in the person of the Bishop of London.

The toast was acknowledged by the Right Rev. the Lord Bishop of London, who humorously enquired whether the hosts could really be so keen about the good health of the guests and how the College could prosper if the guests were not from time to time in need of the professional assistance of the hosts. He thanked the College most gratefully for their "glorious hospitality."

Sir Archibald McIndoe (Vice-President) proposed the health of the Hunterian Orator, praising him for following so rightly in the footsteps of John Hunter. He traced Sir Reginald Watson-Jones' distinguished career since he had determined at the age of thirteen to become an orthopaedic surgeon and had later come so closely under the influence of Sir Robert Jones.

Sir Reginald Watson-Jones, although protesting that he had already put out his best endeavour once that day, made a graceful and interesting reply.

The guests at dinner, though much depleted by the current epidemic of influenza, numbered 130, and in addition to those already mentioned included the Lord Chancellor, the French Ambassador, the High Commissioner for South Africa, the Duke of Devonshire, the Chancellor of the Exchequer, the First Lord of the Admiralty, the Minister of Health, the Treasurer of Lincoln's Inn, the Vice-Chancellor of the University of London, the President of the Royal Academy and many others holding distinguished positions in the land and many notable benefactors of the College.

APPOINTMENT OF FELLOWS AND MEMBERS TO CONSULTANT POSTS

B. N. COLABAWALLA, M.B., F.R.C.S.	Consultant Surgeon to Masina Hospital, Bombay, and Consultant Urologist to S. K. Patil Arogydham Hospital, Malad, Bombay.
J. A. G. HOLT, F.R.C.S., F.F.R.	Consultant Radiotherapist to Peter McCallum Clinic, Melbourne.
K. L. BARNES, F.R.C.S.	Consultant Orthopaedic Surgeon and Surgeon Superintendent to Wrightington Hospital.

The Editor is always glad to receive details of new appointments obtained by Fellows and Members, either through the Hospital Boards or direct.

SIR HARRY PLATT, Bt.

DURING HIS VISIT to India, Pakistan and Ceylon, Sir Harry Platt visited Lahore. The following is the Address of Welcome to Sir Harry which was read, on behalf of Fellows and Members of the Royal College of Surgeons of England working in Lahore, by Dr. Riyaz-i-Qadeer, F.R.C.S., Professor of Clinical Surgery, King Edward Medical College, Lahore.

" Dear Sir Harry Platt,

We, Fellows and Members of the Royal College of Surgeons of England working in Lahore, deem it a great privilege to extend to you a most cordial welcome on the occasion of your memorable visit to this ancient and historic city—the oldest and largest centre of Scientific Medical Education in Pakistan. The capital of West Pakistan with its magnificent historical monuments is not only the seat of the oldest and largest University and Medical College in Pakistan, but is also rich in institutions for all types of Oriental and Occidental Learnings. Lahore has invariably been the educational and cultural nerve-centre of the north-west region of the Indo-Pakistan Sub-Continent and has always enjoyed an enviable reputation for its literary and scientific pursuits.

" Since the establishment of Pakistan it has been our good fortune to greet distinguished visitors from The Royal College of Surgeons of England. The great leader and teacher of surgery, eloquent orator and renowned writer, Admiral Sir Gordon Gordon-Taylor, K.B.E., C.B., M.A., M.S., F.R.C.S., F.A.C.S., Past Vice-President of the Royal College of Surgeons of England, visited twice : first in January 1951, and again in October 1952. It is a matter of great pride for us that the Immediate Past President of the Royal College of Surgeons of England is gracing this meeting with his presence. Visits such as these revive happy memories of our valuable association with the Royal College of Surgeons of England and are a source of no small encouragement and inspiration to us. We are very fortunate, indeed, in having in our midst a great teacher of the University of Manchester, the Master Orthopaedic Surgeon and the President of the International Society of Orthopaedic Surgery and Traumatology, whom some of us had known only through his works as an international authority on Orthopaedic Surgery, particularly on congenital dislocation of the hip and on the peripheral nerve injuries, the co-originator of the Putti-Platt operation for recurrent dislocation of shoulder and as an illuminating author of sections in famous standard works on operative surgery—to mention only a few achievements. It falls to the lot of only a selected few to be so honoured abroad as well as in their own countries, as you, Sir Harry Platt, have been. So great has been the appreciation of your valuable work that the three eminent Universities of Manchester, Liverpool and Belfast have conferred on you the Degree of Doctor of Laws. In 1954 you earned the highest honour on your election as the President of the Royal College of Surgeons of England. You, Sir Harry Platt, were the first Orthopaedic Surgeon and the third person from

outside the Metropolitan London to be elected to that august office and to wear the insignia thereof. A number of Commonwealth countries and the United States of America have honoured you by conferment of Honorary Fellowships of their Colleges. Your marvellous achievements have earned for you the unique distinction of being the First President of The Federation of Colleges of Surgeons of the World—a richly-deserved appreciation of your wonderful achievements in the domain of Medical Science.

"We, Fellows and Members of the Royal College of Surgeons of England, working in this part of the world, are upholding, in our humble and modest way, the noble traditions and high ideals of the Parent Body. The Annals of the Royal College of Surgeons of England do keep up our link with the Parent Body, but we are looking forward to a more concrete liaison with the Royal College in London. It is our earnest request that you will very kindly convey our best wishes and compliments to President Sir James Paterson Ross and Members of the College Council and we fervently hope that this auspicious visit of yours will prove beneficial to us in more ways than one.

"We hope that you, Sir Harry Platt, will enjoy your short stay at Lahore and we sincerely wish you a safe and enjoyable return journey."

FELLOWS' ANNUAL SUBSCRIPTIONS UNITED KINGDOM INCOME TAX RELIEF

THE ROYAL COLLEGE of Surgeons of England has been approved by the Commissioners of Inland Revenue for the purposes of Section 16, Finance Act, 1958, under which an annual subscription to an approved body is allowable as a deduction from the emoluments of any office or employment assessable to United Kingdom income tax under Schedule E.

This approval brings United Kingdom income tax relief to:

A Fellow who is a compulsory subscriber to the College or to

Any other Fellow who pays an annual subscription to the Annals of the College (known to the Commissioners of Inland Revenue as the College's Journal).

The term "Fellow" includes a Fellow in Dental Surgery or in the Faculty of Anaesthetists.

A Fellow who is a compulsory subscriber may claim the whole of his annual subscription (at present five guineas) as an allowable deduction.

Any other Fellow who pays an annual subscription to the Annals may claim this subscription (at present £2) as an allowable deduction.

A voluntary annual subscription to the College is not eligible for deduction.

The Senior Principal Inspector of Taxes has outlined the circumstances and manner in which claims can be made in a letter to the College dated 3rd February 1959, and bearing the reference C.I./SUB/518/LACH. Fellows may wish to quote this reference when making claims.

The relevant passages of the letter read as follows :

" Commencing with the year to 5th April, 1959, a member who is assessable to income tax under Schedule E in respect of the emoluments of an office or employment is entitled to a deduction from those emoluments of the whole of the annual subscription which is due and payable by him to the society in the income tax year provided that :

(*a*) the subscription is defrayed out of the emoluments of the office or employment."

A member of the society who is entitled to the relief should apply to his tax office as soon as possible for form P.358 on which to make a claim for adjustment of his pay-as-you-earn coding.

LIFE IN EMERGENCY WARD 10

MANY OF OUR Fellows must be aware of the publicity now being given to the College and its affairs by the Press, the radio and television. This departure from our customary reticence has been advised by the Public Relations Sub-committee of the College Appeal Committee who believe that it is important for the public to be well informed about how the College is striving to promote the science and art of surgery by setting high standards in postgraduate education and training, and by extending the research activities of its various scientific departments.

Through the kindness of certain members of the Appeals Committee and the generosity of Eros Films Ltd., the première of the film version of the popular television feature " Life in Emergency Ward 10 " was given to an invited audience in the Great Hall of the College on the evening of March 24th.

" Life in Emergency Ward 10 " is first-class entertainment, for it is amusing, dramatic and instructive. Though the hospital situations have to be somewhat over-emphasised to make them dramatically satisfying yet their portrayal is wonderfully true to life ; and the chief episode in the film, the circumstances leading up to a risky operation on an apparently healthy child, is very cleverly worked out. The clinical problem, which has not only to be thought out by the surgeons but also explained to the anxious parents who have to make the final decision, is familiar to all of us, and is handled with great understanding and skill. And running throughout the film, for those who care to think what lies behind the picture itself, is the influence of scientific research upon surgical practice.

To those who arranged for this film première to be given in the College we owe a very great deal, for it enabled us officially to launch our Appeal. It is going to be a gigantic task to raise all the money needed to complete our buildings and then to maintain the educational and research activities in the expanded departments, but the film première should have given us a good start, for it must have interested a large number of people in the welfare of the College.

Professor Bourne-Evans (Wilfred Hyde White) head of the doctors who are assisting him in a serious heart operation; Mr. Alan Dawson (Charles Tingwell); Dr. Tom Hunter (Rupert Davies); and an assisting nurse watch tensely the operative progress of a new heart-lung machine modification. Beneath the glare of the operating theatre lights they work in silence.

As Dr. Stephen Russell (Michael Craig) listens tensely to the beating of a small boy's heart, Professor Bourne-Evans (Wilfred Hyde White) head of the Oxbridge Hospital, kindly humours the sick child. It has been diagnosed that the child has a hole in his heart and a serious operation imminent.

SOMMÉ'S MANUSCRIPT REPORT ON A CASE OF FUNGOID DISEASE OF THE GUMS AND UPPER JAW (MADAME DE HARVEN), WITH COPIES OF CONSULTATIONS BY ROUX, BOYER AND DUPUYTREN

edited and translated by

Claude H. Fleurent, L.-ès-L.

Chief Library Assistant, Royal College of Surgeons of England

BORN IN PARIS on 8th April 1772, Claude-Louis Sommé studied medicine at the Charité and Hôtel-Dieu, and started his career as " chirurgien sous-aide " with the army of the Rhine. Frequent changes of garrison and an appointment over the head of Larrey to a post of " chirurgien de première classe " at the Val-de-Grâce mark the first period of his professional life. He took his doctorate at Strasbourg on 8th April 1806, and relinquished his commission when the mayor of Antwerp, who had had the opportunity of appreciating his merit at the time of the French occupation, offered him the post of Surgeon-in-Chief at the Hôpital Sainte-Elizabeth. He also became professor at the Antwerp School of Medicine, where he taught pathology and operative medicine. He died in Antwerp in 1854.

A member of the Société d'Émulation d'Anvers since 1804, he was elected an associate of the Académie des Sciences de Bruxelles in 1843 and a member of the Académie Royale de Médecine de Belgique in 1847, and took part in the activities of many other societies, including the Société Linnéenne de Paris. It is to this interest in botany and horticulture that we owe the creation of the splendid botanical garden of Antwerp. His fame and esteem among his fellow-citizens were just as great. He was summoned in the most desperate cases and for the most difficult operations, and one of his patients was Madame de Harven, the subject of this report.

" Madame de Harven[1] s'est plaint depuis plusieurs années de douleurs aux dents de la machoire superieure a la suite des quelles, il est survenu du gonflement aux gencives de l'arcade alveolaire superieure, elle a été traitée pendant quelque temps par un dentiste de Bruxelles. La tumefaction et la douleur augmentant, et les dents superieures incisives et canines etant devenues mobiles, Mad. de H. prit l'avis du soussigné auquel fut adjoint

[1] "According to the death certificate of the 12th March 1835, Marie Ange van den Bergh, aged 38 years, 11 months and 2 days, born in Antwerp, daughter of Jean Jacques and of Marie Françoise Aerts, wife of Alexander Joseph de Harven died in Antwerp of ' haematoid fungus.' In the act the disease is described as ' fongus hematode ' but Dr. P. Janssens, a medical officer of the city of Antwerp, informs me that, in his opinion, the clerk must have misspelt the word " (Blockmans).

Mr. Baud[2] professeur a Louvain. Comme il etoit question d'operation, avant de s'y decider, elle partit pour Paris. elle s'adressa a Messieurs Roux et Boyer et a Mr. Dupuytren. Voici la copie de leurs consultations —

1ere

Les soussignés après avoir examiné attentivement et a plusieurs reprises Mad. de H. ont acquis la conviction qu'elle etoit affectée d'un[e] veritable epulis, ou degenerescence fongueuse du tissu des gencives [.] ils sont persuadés que cette maladie maintenant bornée a une portion du rebord alveolaire de la machoire superieure pourroit faire des progrés ulterieurs [,] que bien certainement au moins, elle n'est pas susceptible de retrograder et que si Mad. de H. veut être delivrée des incommodités dont cette affection est la source, elle doit se resourdre a subir une operation dont le but seroit d'enlever les parties molles et même une portion du rebord alveolaire [.] Si on trouvoit les os malades au dessous de la masse fongueuse, on devroit faire succeder l'application du cautere actuel a l'ablation des parties malades.

Dans le cas ou madame de H. auroit une repugnance insurmontable pour une operation qui pourtant seroit la seule voie de guerison, elle devra se borner a faire plusieurs fois par jour sur la partie malade des lotions avec de l'eau de joubarbe et de suc de laitue melées a parties egales.

Paris le 30[3] juillet 1833
Signés—Roux et Boyer[4].

2eme

il est fortement a craindre que la maladie que Made. porte a la partie anterieure de la machoire superieure soit de nature cancereuse et qu'elle ne puisse être guerie que par l'ablation de toute la partie de gencives et d'os malades.

Cependant je desirerois avant d'entreprendre cette ablation 1° qu'un seton fut appliqué a la partie posterieure du col pour être entretenu pendant plusieurs mois—2° qu'il fut fait pendant le même temps en trois

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[2]Jean-Marie Baud (1776-1852) followed a career similar to Sommé's. Having remained in Antwerp after the withdrawal of the French army, he became, in 1817, professor of anatomy and surgery at the State university of Louvain, a post which he held until the revolution of 1830, when the Catholic Church reclaimed the university which she had founded in 1425. A modest but distinguished teacher, whose intuition was always justified by his subsequent achievements, he was one of the first three men of science to receive a decoration in Belgium. He was held in the same high esteem by the Académie Royale de Médecine de Belgique and by the foreign societies who admitted him to their membership. In his adopted city of Antwerp, Baud became the friend of the population, and he served on the municipal council from 1835 to 1843. His contribution to medical literature is small but remarkable by the co-ordination of ideas and the elegance of his style. His main work, Pathologie Chirurgicale, was never published, as he was engaged on the revision of the manuscript at the time of his death.

[3]The manuscript gives the date as 30 with a 1 over the 0.

[4]For information on Roux and Boyer, see the Author's article on Early visitors to the Museum of the Royal College of Surgeons of England and Philibert Joseph Roux's account of his own visit on 21st August 1814. (Ann. Roy. Coll. Surg. Engl. July, 1958 **23**, 47).

ou quatre fois par jour des lotions et des injections avec de l'eau alumineuse —3° enfin qu'il fut donne des antiscorbutiques et des astringens sous toutes les formes.

Ces moyens seront mis en usage pendant longtemps et jusqu'a complette guerison, s'ils amènent une amelioration sensible dans l'etat du [sic] malade [.] ils seront suspendus et on auroit recours a l'extirpation de la machoire superieure si au bout d'un mois, ils n'avoient pas empeché le mal de s'accroitre.

On devrait regarder comme une amelioration alors même qu'il y auroit augmentation dans le gonflement des gencives la formation d'une nécrose, car alors on pourroit esperer de voir le mal des gencives guerir après la chute, l'expulsion ou l'extraction de l'os malade, et c'est la-dessus que se fonde mon principal espoir [.]

Paris 30 juillet 1833
Signé Dupuytren.

Mad. de Harven s'etant refusé a l'operation, de retour a Anvers, elle se mit de nouveau sous le traitement du soussigné et d'aprés l'avis de Mr. Dupuytren, on mit un seton a la nuque, et on appliqua sur le mal de l'alun calciné pour obtenir plus promptement le dessechement des excroissances produites par les vegetations du carcinome des gencives. Les dents mobiles furent retirées. L'arcade alveolaire entierement detruite par la carie des os maxillaires superieurs, ne pouvoit soutenir ces dents, qui du reste etoient parfaitement saines, on employa ensuite une poudre caustique avec laquelle on parvint a detruire une portion des gencives, mais la maladie faisant de nouveaux progrés, Mad. de H. s'est decidée a se rendre a Londres[5] pour y prendre des avis sur les moyens a employer pour sa guerison.

Anvers ce 10 8bre 1833
Sommé DM "

" Madame de Harven has complained for several years of pain in the teeth of the upper jaw as a result of which, there followed a swelling of the gums of the upper alveolar process, she has been for some time treated by a dentist of Brussels. The swelling and pain increasing, and the upper canine and incisive teeth having become loose, Mad. de H. sought the advice of the under-signed in joint consultation with Mr. Baud, professor at Louvain. As an operation was mentioned, before she agreed to it, she set off for Paris. She applied to Messieurs Roux and Boyer and to Mr. Dupuytren. Here is the copy of their consultations —

1*st*

The undersigned after having examined Mad. de H. attentively and on several occasions have decided that she was suffering from a true epulis, or fungoid degeneration of the tissues of the gums[.] they are convinced

[5]The medical journals published in London between 1833 and 1835 contain no report of Madame de Harven's case.

that this disease now limited to a portion of the alveolar process of the upper jaw could progress subsequently[,] that most certainly at least, it is not likely to subside and that if Mad. de H. wishes to be rid of the inconveniences of which this affection is the source, she must be resolved to submit to an operation the aim of which would be to remove the soft tissues and even a portion of the alveolar process[ ] If diseased bone was found beneath the fungoid mass, the application of an actual cautery should follow the excision of the diseased part.

In case Madame de H. felt an uncontrollable repugnance to an operation which would nevertheless be the only means of recovery, she will have to content herself with bathing the diseased part several times a day with houseleek water and lettuce juice mixed in equal parts.

Paris 30th July 1833
Signed—Roux and Boyer.

2nd

it is to be greatly feared that the disease from which Made. suffers in the anterior part of the upper jaw be cancerous in nature and that she might not be cured except by the excision of the entire area of diseased gums and bones.

I should however before undertaking this operation recommend 1° that a seton be applied to the posterior part of the neck and left in place for several months—2° at the same time that a solution of alum be used three or four times a day for bathing and for injections—3° finally that anti scorbutics and astringents be administered in all forms.

These measures will be applied for a long time and until complete healing, if they procure a marked improvement in the condition of the patient[.] they will be suspended and one would resort to the extirpation of the upper jaw if after one month, they had not prevented the disease from increasing.

One should consider the formation of necrosis as an improvement even in the presence of increased swelling of the gums, since one could then hope to witness the healing of the lesion of the gums following the fall, the expulsion or excision of the diseased bone, and therein my hope chiefly lies[.]

Paris 30th July 1833
Signed Dupuytren.

Mad. de Harven, having refused the operation and having returned to Antwerp, placed herself once more under the care of the undersigned and according to the advice of Mr. Dupuytren, a seton was applied to the nape of the neck and burnt alum to the lesion in order to hasten the desiccation of the excrescences produced by the vegetations of the carcinoma of the gums. The loose teeth were removed. The alveolar process entirely destroyed by the caries of the upper maxillary bones, could not support those teeth, otherwise perfectly sound, one then used a caustic

powder with which one succeeded in destroying part of the gums, but the disease making further progress, Mad. de H. has resolved to proceed to London in order to seek advice on the means to employ for her recovery.

Antwerp this 10th 8ber 1833
Sommé DM"

The title "Fungoid disease of the gums and upper jaw," appears in the top right-hand corner of the fourth and last page of the manuscript. Immediately underneath one can decipher this prescription:

" C[h]lorine, Sub[murias] Hyd[rargyri] c[um] opio.
Dec[octum] Sars[aparillae] C[ompositum] "

Letters u and b of Sub. are illegible, but an interpretation was offered by Jourdan's *Pharmacopée Universelle, ou Conspectus des Pharmacopées* (Paris, 1828), a book which Sommé and his colleagues must have known. Jourdan prescribes a "mixture antisyphilitique," consisting of "submurias hydrargyri cum opio" and conserve of roses, to be administered with orgeat and a concentrated decoction of guaiacum. Further on, he lists compound decoction of sarsaparilla and compound decoction of guaiacum as being equivalent medicines. All this, and the use of chlorine, indicate that Madame de Harven's lesion was probably due to syphilis.

ACKNOWLEDGMENTS

I wish to express my gratitude to Professor dr. F. Blockmans, City Archivist, Antwerp, who supplied information on Madame de Harven, to Mr. W. R. LeFanu, M.A., Librarian of the College, for his generous advice and for his permission to publish this manuscript, and to Miss A. Lothian, F.P.S., A.L.A., Librarian, Pharmaceutical Society of Great Britain, who helped me to decipher the formulae on page 4 of this manuscript.

NOTE.—The spelling and accents in the text agree with the manuscript.

REFERENCES

BLOCKMANS, F. (1958) Personal communication.
JOURDAN, A. J. L. (1828) *Pharmacopée Universelle, ou Conspectus des Pharmacopées* Paris, Baillière.
SAUVEUR, D. J. J. (1855) *Bull. Acad. Méd. Belg.* **15**, 2. (Notice sur M. le docteur Sommé).

LIFE OF SIR GEORGE BUCKSTONE BROWNE, F.R.C.S.

A BIOGRAPHY HAS been written of Sir George Buckston Browne, one of the greatest benefactors the College has had, by Miss Jessie Dobson, B.A., M.Sc., and Sir Cecil Wakeley, Bt., K.B.E., C.B., LL.D., F.R.C.S. The publishers are Messrs. E. & S. Livingstone and the price of the book is 25s. net.

PROCEEDINGS OF THE COUNCIL

AT A MEETING of the Council on 12th March 1959, with Professor Sir James Paterson Ross, President, in the Chair, Mr. G. H. Macnab (Westminster Hospital) was admitted to the Court of Examiners. Mr. Gordon Paul, of Bristol, was admitted to the Fellowship *ad eundem*.

The Hallett Prize was presented to G. R. Duncan of the University of Otago, New Zealand.

The Handcock Prize was presented to J. C. Bull of Guy's Hospital Medical School.

The 28th Macloghlin Scholarship was awarded to Peter Beck of Wyggeston Boys' School, Leicester.

Diplomas were granted as follows: *Membership* (1), *Licence in Dental Surgery* (73), *Fellowship in the Faculty of Anaesthetists* (3).

The following hospitals were recognised under paragraph 23 of the Fellowship Regulations:

Hospitals	Posts Recognized		
	General (6mths. unless otherwise stated)	Casualty (all 6mths.)	Unspecified (all 6mths.)
Wolverhampton—Royal Hospital (Additional)		S.H.O.	
	Continuation of temporary recognition until March 1st 1960		
London — German Hospital, Dalston	S.H.O.	Cas. Off. (S.H.O.)	
		Continuation of temporary recognition until January 1st 1960	
Hertford — Hertford County Hospital		Cas. Off.	
			Confirmation of temporary recognition under paragraph 23 (c) E.N.T. Registrar
Wigan—Royal Albert Edward Infirmary			
Barnet—Clare Hall Hospital (redesignation)			*Redesignation of* S.H.O. as Registrar
Periods of recognised training in the following Ophthalmological posts to be extended from 6 to 12 months.			
Huddersfield — Royal Infirmary		Registrar	
Hull—Royal Infirmary		House Surgeon	
York—County Hospital		House Surgeon	

CARDIAC SURGERY

SIR RUSSELL BROCK'S Bradshaw Lecture of 1957 on *The present position of cardiac surgery* is now available in blue cloth binding, price 6s. a copy, from the following booksellers:

Baillière, Tindall and Cox Ltd., 8, Henrietta Street, Covent Garden, W.C.2.

H. K. Lewis and Co. Ltd., 136, Gower Street, W.C.1.

Lloyd-Luke (Medical Books) Ltd., 49, Newman Street, W.1.

BINDING OF THE ANNALS

BINDING CASES ARE not provided for completed volumes of the ANNALS but the Editor can recommend the firm of Lovett, Bookbinders, 86, Plashet Grove, London, E.6, who will undertake the binding in buckram or leather to individual requirements at reasonable prices.

DIARY FOR APRIL

Wed. 22		Second L.D.S. Examination begins.
Thur. 23		Association of Surgeons Annual Meeting.
Fri. 24		Surgical Lectures and Clinical Conferences end.
		Association of Surgeons Annual Meeting.
	4.30	PROF. J. H. LOUW—Moynihan Lecture—Observations on the pathogenesis and treatment of congenital intestinal atresia.*
Sat. 25		Association of Surgeons Annual Meeting.
Mon. 27		Dental Lectures and Clinical Conferences begin.
Tues. 28		Final Fellowship Examination (Ophthalmology and Otolaryngology) begins.
	3.45	MISS J. DOBSON—Arnott Demonstration—John Hunter's Museum.*
	5.00	MR. T. WARD—Fractures of the facial bones—I.
	6.15	DR. L. FORMAN—Oral manifestations of skin diseases—I.
Wed. 29	5.00	J. D. FERGUSSON—Institute of Urology Lecture—Cysts of the kidney.*
Thur. 30	5.00	MR. T. WARD—Fractures of the facial bones—II.
	5.30	PROF. M. A. RUSHTON—Otolaryngology Lecture—Cystic conditions.*
	6.30	DR. L. FORMAN—Oral manifestations of skin diseases—II.

DIARY FOR MAY

Fri. 1		Last day for application for Lectureships.
	5.00	PROF. JOHN HADFIELD—Hunterian Lecture—Hormone deprivation in breast cancer spontaneously arising or surgically induced.*
Sat. 2		Scientific Meeting of the Faculty of Anaesthetists—Neuro-muscular junction.
Tues. 5		Voting papers for Council issued.
		Final Fellowship Examination (General Surgery) begins.
	5.00	DR. W. CAMPBELL—Radiology of the Facial Bones—I.
	6.15	MR. J. WATSON—Head injuries.
Thur. 7		D. A. Examination and D. Path. Examination begin.
	5.00	DR. W. CAMPBELL—Radiology of the Facial Bones—II.
	5.00	DR. K. M. BACKHOUSE—Arris & Gale Lecture—The gubernaculum testis hunteri, testicular descent and maldescent.*
	6.15	MR. V. E. IRELAND—Disorders of the mandibular joint.
Fri. 8		Basic Sciences Lectures and Demonstrations end.
Tues. 12	5.00	MR. B. COHEN—Secondary tumours of the jaws.
	6.15	DR. M. F. J. MCARDLE—facial pain.
Thur. 14	2.00	Ordinary Council.
	5.00	PROF. M. A. RUSHTON—Lesions of the tongue.
	6.15	MR. C. R. MCLAUGHLIN—The cleft palate.
Fri. 15	5.00	Board of Faculty of Dental Surgery.
Sat. 16		College closed.
Mon. 18		Whit Monday. College closed.
Tues. 19	5.00	MR. H. C. KILLEY—The maxillary antrum in relation to dental surgery.
	6.15	MR. S. H. WASS—Osteomyelitis of the jaws.
Thur. 21	5.00	PROF. E. D. FARMER—Oral ulcers.
	6.15	MR. B. W. FICKLING—Surgical correction of deformities of the jaws.
Fri. 22	5.00	THE RT. HON. LORD COHEN OF BIRKENHEAD, M.D., F.R.C.P.—Charles Tomes Lecture—Facial neuralgias.*
Tues. 26		Last day for nomination of candidates (L.D.S.) for election to the Board of Faculty of Dental Surgery.
Tues. 26	5.00	MR. B. E. D. COOKE—Fibro-osseous swelling of the jaws—I.
	6.15	PROF. R. B. LUCAS—Pathology of oral neoplasms—I.
Thur. 28	5.00	MR. B. E. D. COOKE—Fibro-osseous swelling of the jaws—II.
	6.15	PROF. R. B. LUCAS—Pathology of oral neoplasms—II.

*Not part of lecture course.

5

THE SURGERY OF ANASTOMOTIC ULCERATION

Hunterian Lecture delivered at the Royal College of Surgeons of England on 8th May 1958

by

W. W. Davey, M.D., F.R.C.S., F.R.C.S.(I.)

Consultant Surgeon, Whittington Hospital, London*

A MARK OF an experienced gastric surgeon is his ability to diagnose the anastomotic ulcers which follow his own operations or the operations of other surgeons. Even in this age of technical "know how," diagnosis still precedes treatment. Once diagnosed, the surgical treatment of anastomotic ulceration is beginning to follow certain definite lines.

The emphasis of this lecture will fall on diagnosis. Its facts have their foundation in the clinical stories and investigation of eighty-seven patients observed during the past eight years.

What is the magnitude of the problem ?

In the large community hospital in which this work was done, we do between us over 200 partial gastrectomies for peptic ulceration each year. The hospital serves a quarter of a million people ; assuming the same rate for the rest of Britain's population of 50,000,000, then 36,000 stomachs are taken out of the abdominal cavity each year, 3,000 a month, 100 a day.

Every quarter of an hour one of our patients loses part of his stomach.

Supposing these 36,000 specimens were placed end to end, they would stretch from Buckingham Palace to St. Paul's Cathedral following the Royal Route.

It is commonly accepted that over half of these gastrectomies are done for duodenal ulceration, and at least four in every hundred will develop a further anastomotic ulcer. If we add to this the anastomotic ulcers which continue to be found in these the third and fourth decades following the "hey-day" of gastro-enterostomy, we can therefore expect well over 1,000 new patients with this lesion each year.

CLASSIFICATION

These anastomotic ulcers fall naturally into the following groups.

TABLE I

ANASTOMOTIC ULCER

ANALYSIS

Total .. 87

Male 76. Female 11. Age range 22-84

GROUPS

Polya	40
Gastro-enterostomy	34
Billroth I	8
Gastro-jejuno-colic	5

You will notice there are only eleven anastomotic ulcers in women, eight of which followed gastro-enterostomy.

Lastly, comment will be made on a group who have been subjected to surgery in whom no anastomotic lesion was found.

* Now Professor of Surgery, University College, Ibadan, Nigeria.

THE POLYA GROUP

TABLE II

Anastomotic Ulcer. Polya Group. 40

PRESENTATION

Pain	26
Haemorrhage	20
Perforation	7

Pain is the great symptom which brings peptic ulcer patients to their doctors. There is no exception to this in the case of anastomotic ulcers, even though the surgeon has grossly altered the anatomy of the foregut and disrupted its nervous pathways. Figure 1 maps the localization of pain which was present in two out of every three patients.

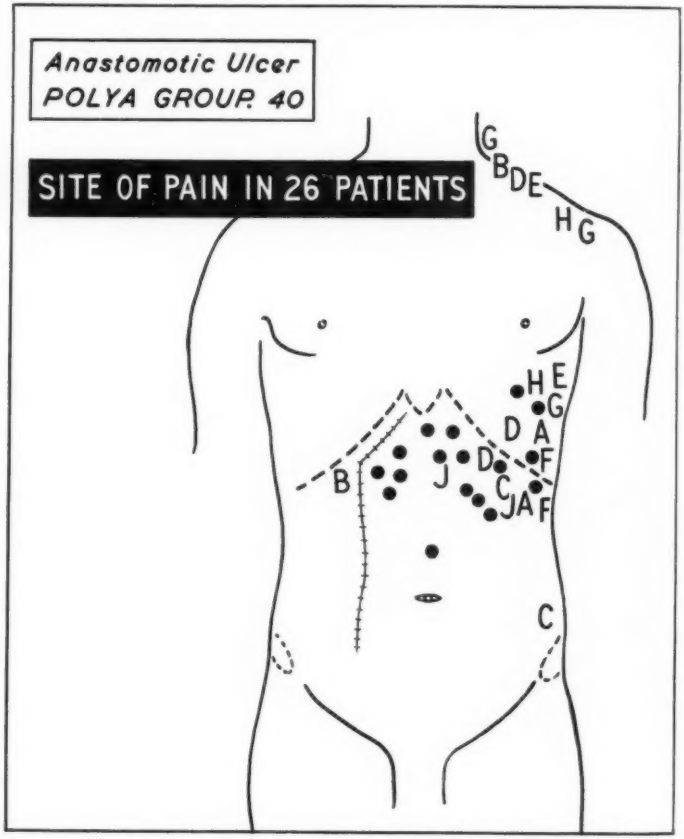

Fig. 1. Where letters are used it indicates that the patient has pain in more than one area.

You will see from a study of the chart that the pain falls into two areas. On the one hand the patient complains of epigastric pain, and may even volunteer that his old ulcer pain has returned. It would be nice in these cases to believe there is such a thing as " phantom " ulcer but, alas, the patient is nearly always right ; his ulcer has returned. On the other hand he may complain of symptoms suggesting a lesion of the left chest and shoulder. Should these symptoms develop soon after his Polya gastrectomy —and our earliest was less than six weeks—then it is likely that a cause for the pain may be sought below the diaphragm.

But if there is a reasonable time interval, and the average in this series was twenty months, the diagnostic ball may be set rolling in the wrong direction, for example :

A male patient who had had a Polya gastrectomy for duodenal ulcer eleven months previously, complained persistently of pain in the left

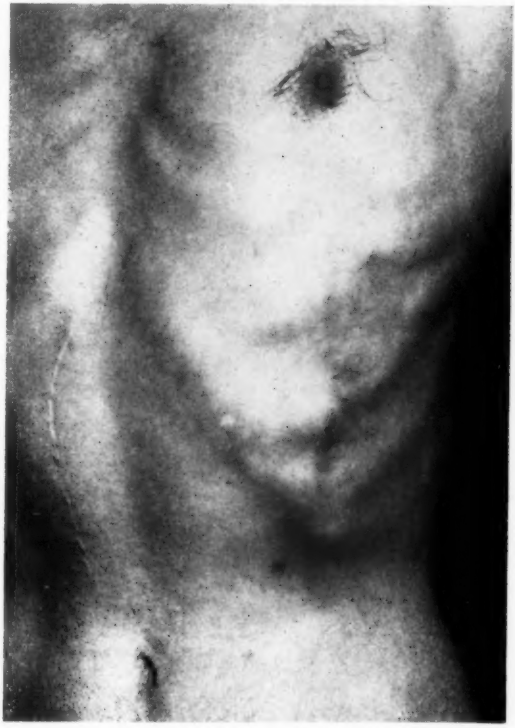

Fig. 2. Notice pigmentation of the skin from the repeated application of a hot water bottle and a right paramedian incision used for the Polya gastrectomy.

shoulder. On examination there was crepitus in the joint and an X-ray showing calcification in the supraspinatus tendon further helped to focus attention on this region. He was receiving physiotherapy before it was realised that his pain was due to a large anastomotic ulcer penetrating the underside of his left diaphragm.

Yet another patient complained of constant severe pain in the left upper quadrant of the abdomen, for which he was taking aspirin every half-hour. He became emotional and wept more and more as his doctors appeared to understand him less and less, and finally he brought matters to a head when he drank a whole bottle of " Carbrital " in an attempt to gain relief. The base of his ulcer had become part of the periphery of his diaphragm.

Granted the history of a previous Polya gastrectomy for duodenal ulcer, Figure 2 should almost be pathognomonic of an anastomotic ulcer penetrating the left diaphragm.

Fig. 3. Shows clearly the crater of a large penetrating ulcer in the efferent jejunum of an ante-colic Polya gastrectomy.

Haemorrhage

TABLE III

Anastomotic Ulcer. Polya Group. 40

HAEMORRHAGE

Total .. 20

Melaena	15
Melaena and Haematemesis	4
Haematemesis	1

In half of the patients there was haemorrhage and this was nearly always in the form of melaena. In five patients the melaena was silent. All of the patients got better without emergency surgery.

Perforation

TABLE IV

Anastomotic Ulcer. Polya Group. 40

PERFORATIONS 8

Average Time after Gastrectomy = 15 months

The gastrectomist is not kept waiting long for his perforated anastomotic ulcers, the earliest occurred in less than five months, and the latest in three and a half years, while in a man of seventy-one it took just over a year. An accurate pre-operative diagnosis was made in every case except

Fig. 4 (*a*). The efferent jejunum is deformed and stenosed immediately distal to the stomach.

Fig. 4 (*b*). "Tea pot" like deformity of the proximal jejunum due to shortening at the site of the ulcer and

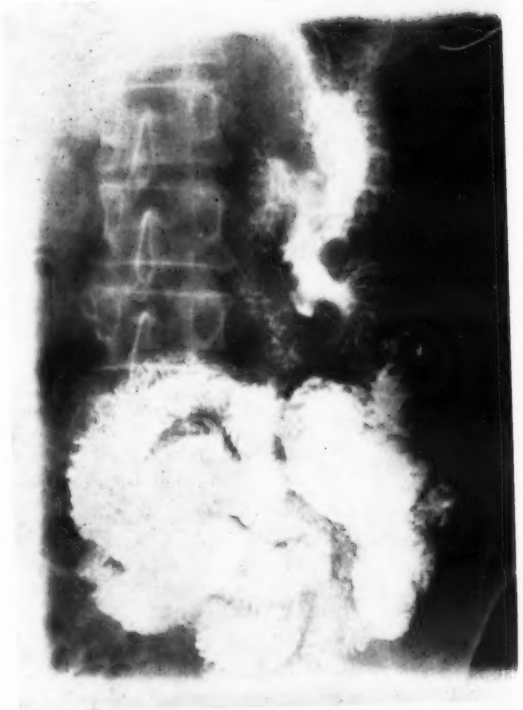

Fig. 4 (*c*).
Ulcer crater on mesenteric border of jejunum opposite stoma.

Fig. 4 (*c*). Ulcer crater on mesenteric border of ileum opposite stoma.

Fig. 4 (*d*). Adhesion running from base of ulcer to periphery of diaphragm across pneumo-peritoneum.

Fig. 4 (*b*). "Tea pot" like deformity of the proximal jejunum due to shortening at the site of the ulcer and

in one patient, admitted late to a medical ward, the cause of his left pleural effusion, his left lower lobe atelectasis and his left shoulder pain being completely overlooked during his three-month stay in hospital.

With the exception of one, all of the operations to close the perforated ulcers were surprisingly easy, owing to the fact that the anastomoses were of the antecolic type. If there are any surgeons in this audience who have yet to make up their minds as to which is the better—antecolic or retrocolic—this factor alone perhaps might help them to decide.

INVESTIGATION

Barium meal

Written all over Figure 3 are the words, "I am an anastomotic ulcer." It is the radiologist's dream, it shows everything clearly. All too often,

however, the pictures shown need the liberal application of the eye of faith and the reports contain such vaguenesses as "Suggest "," Cannot be excluded," " Stomal tenderness."

How accurate can we expect radiology to be? What are the problems? Can it be improved? Apart from the taking of a good gastric history, it is the mainstay of diagnosis.

Few radiologists can hope to achieve a high level of efficiency in this type of work unless the surgeon gives all the help he can. The most useful information is accurate technical detail about the previous operation. To obtain it, it may be necessary to write or ring up another hospital. This information is all-important; it prepares the radiologist psychologically and sets his mind free to concentrate on finding the ulcer crater rather than unravelling the tortuosities of past surgery.

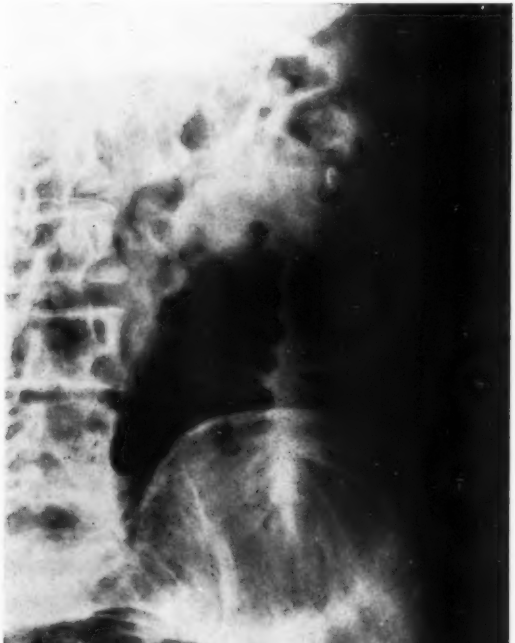

Fig. 5 (*a*). Straight X-ray showing air-filled dilated loop of jejunum.

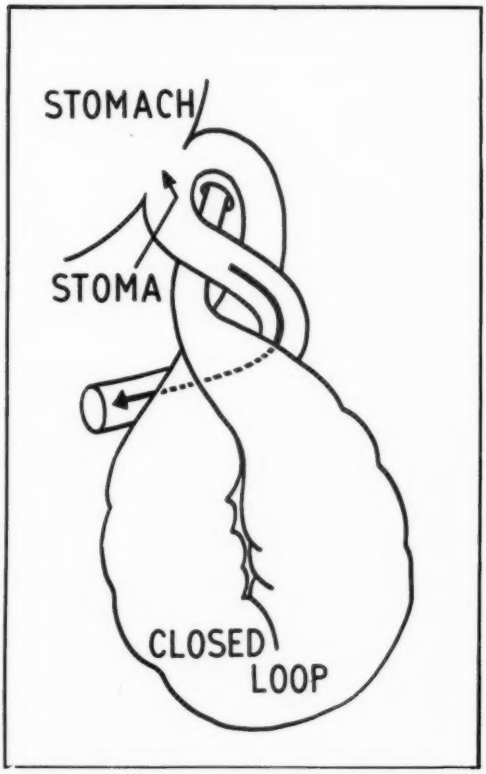

Fig. 5 (*b*). Indicates the mechanism of the obstruction found at operation.

In the average Polya gastrectomy, the gastro-jejunal anastomosis lies above the costal margin and this makes it impossible for the radiologist to palpate the area of the stoma and difficult to get good filling of the efferent loop, as he cannot obstruct the bowel in the flank distal to the anastomosis by direct pressure with his fingers. To help achieve this, we have found it easy to pass a balloon loaded with mercury into the efferent loop, it is then inflated to occlude the lumen, and this allows good proximal filling with barium.

Where the history suggests penetration of the diaphragm, a barium meal coupled with a pneumo-peritoneum may demonstrate the lesion and its attachments.

Using these techniques, with willingness to repeat the examination on several occasions if necessary, and above all providing the radiologist

with all the information we can get, a positive diagnosis has been made in twenty-four out of the thirty-six patients who had barium meals. Figures 4*a*, *b*, *c* and *d*, are examples.

It is possible that the arrival of the image intensifier will lead to great advance in this difficult branch of radiology.

Gastroscopy

TABLE V

Anastomotic Ulcer. Polya Group. 40

GASTROSCOPIES

Total .. 26

Ulcer seen	8
Ligatures seen	1

In one-third of the patients examined by this method, the ulcer was seen. In only two of these was the lesion not seen previously by radiology.

THE GASTRO-ENTEROSTOMY GROUP

TABLE VI

Anastomatic Ulcer. The Gastro-Enterostomy Group. 34

PRESENTATION

Haemorrhage	25
Pain	17
Perforation	3
Palpable lump	2

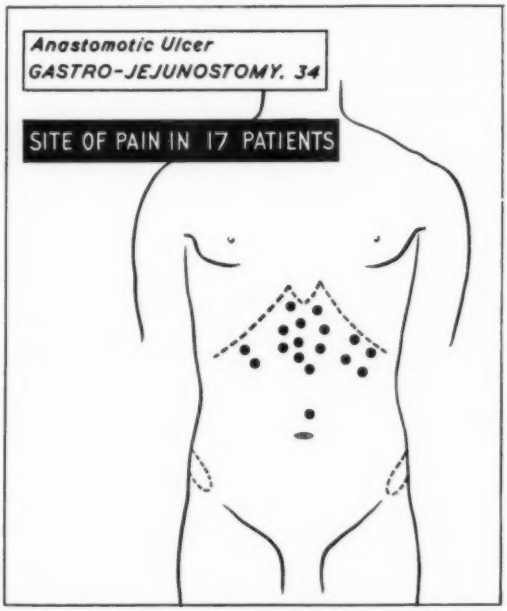

Fig. 6.

In the gastro-enterostomy group of anastomotic ulcers, contrasted with the Polya group, you will see that haemorrhage has changed places with pain as being the commonest symptom. It occurred in three out of four patients.

Haematemesis is as common as melaena and they often occur together. Only on one occasion was emergency surgery needed to control the bleeding and the operation consisted of simple disconnection of the gastro-enterostomy, with repair of the stomach and jejunum.

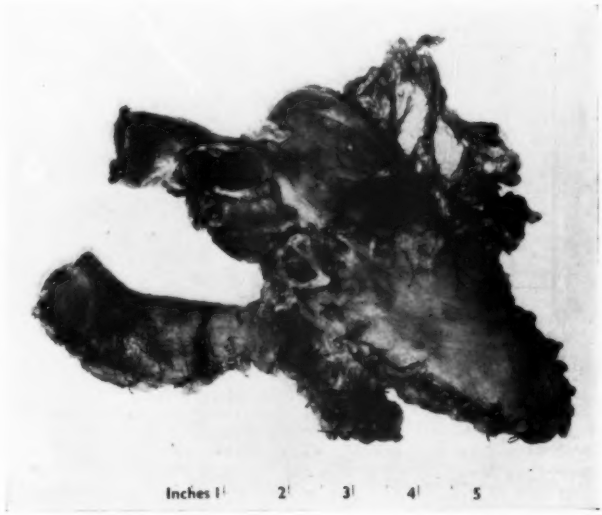

Fig. 7. Resected specimen of double gastro-jejunostomy. The large hole at the commencement of the most distal loop indicates the floor of an anastomotic ulcer which was penetrating the anterior abdominal wall. Beside it in the same loop a second circular ulcer is seen.

In another patient, gastroscopy led to an emergency. Apparently during this examination, the afferent loop, which was too long, was inflated with air, and this caused a closed loop obstruction, a condition so well described by Professor Stammers (Fig. 5*a* and *b*).

Pain occurred in 50 per cent. of patients, its distribution is mapped in Figure 6. Often it was not severe. This is probably due to the fact that the ulcer seldom involved the parietal peritoneum.

On an average an anastomotic ulcer was not diagnosed in this series till over ten years following the initial operation. In one patient it was delayed for thirty-nine years, while the outstanding exception to this late onset was a lady from Cyprus. Perhaps the recent sad happenings in that island had been transmitted to her upper alimentary tract.

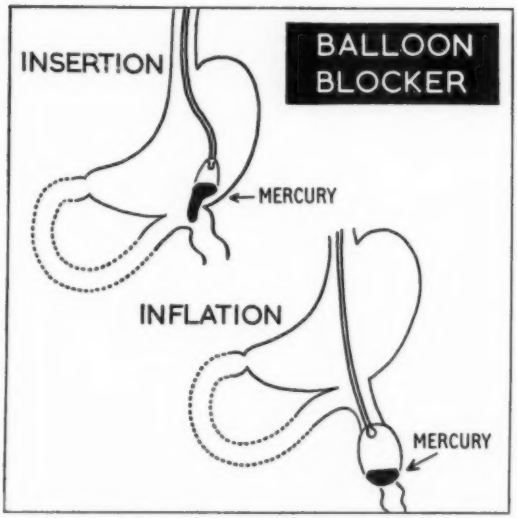

Fig. 8. Once the balloon has reached the efferent jejunum, it is inflated and the barium is given.

I would like to describe this patient, for it shows how vicious these anastomotic ulcers can be. She was admitted a frightened, haunted creature in obvious pain. Unable to speak English, we found out with difficulty that she had had two upper abdominal operations within ten days of each other two years previously. Pain in the epigastrium and back, at the same level, quickly followed these operations and had been continuous and severe ever since.

On examination we found a tender mass in the right upper quadrant of the abdomen. Having had several patients with hydatid cysts from Cyprus, this diagnosis was considered and eliminated. Then an inflammatory mass of the gall bladder was contemplated and ruled out by a normal cholecystogram. A barium meal was difficult to decipher.

At operation a stomach with two gastro-enterostomies, anterior and posterior, was revealed, and two anastomotic ulcers, the larger of which was penetrating the anterior abdominal wall and accounted for the palpable mass. Figure 7 gives a good picture of our findings.

She has now an antecolic Polya gastrectomy and has returned to Cyprus—the emissary of abdominal peace, which I sincerely hope will have widespread radiation.

Of the three patients who presented with perforated gastro-jejunal ulcers, one was an octogenarian, the surgeon who sutured his second perforated duodenal ulcer less than two years previously had compassion

on him and added a short circuit. Fullness of years is no passport to freedom from stomal ulceration.

Confusion often comes from consideration of the decrease of acidity with advancing age, forgetting that mucosal resistance also declines and the end result is still peptic ulceration.

INVESTIGATION

Barium meal

This was carried out in twenty-nine patients. In eighteen of them a definite diagnosis was made. The problems are similar to those of anastomotic ulcer occurring with a Polya gastrectomy and similar methods were used to overcome them.

Figure 8 demonstrates how the Balloon Blocker is used.

Figures 9*a* and *b* illustrate ulcers with the balloon in place, while Figures 9*c* and *d* show ulcers without any special technique. Generally speaking, the wider the stoma the more difficult it is to make a definite

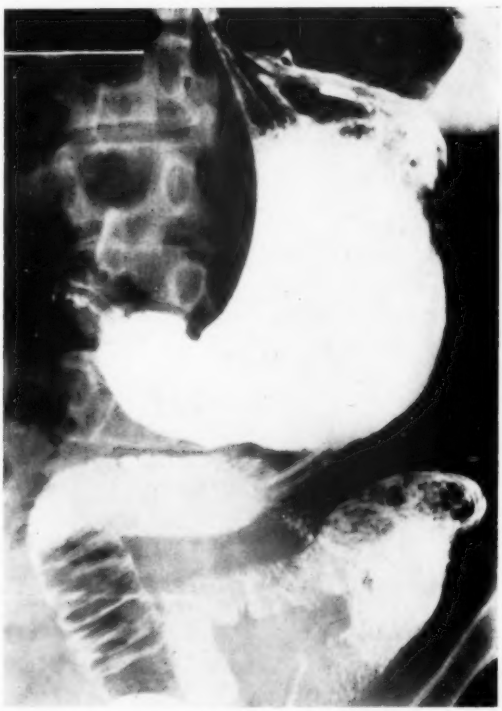

Fig. 9 (*a*). Persistent stenosis of the proximal jejunum with distal inflated balloon and mercury.

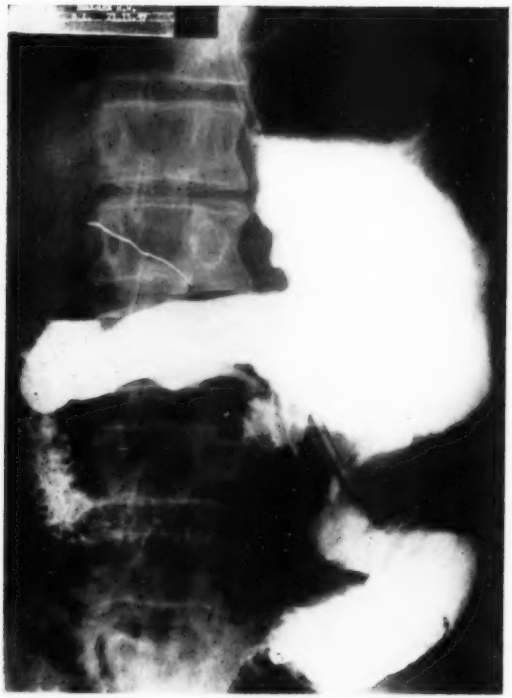

Fig. 9 (*b*). Showing elongated ulcer crater about 2cms. from the stoma, with the upper part of the inflated balloon.

diagnosis. I would like to record my thanks to Dr. Stachurko, who patiently carried out most of these examinations.

Gastroscopy

This was of very little value ; in only two out of twenty-five patients in whom the investigation was carried out was the ulcer seen, and in these patients it had been diagnosed previously by radiology. It has to be remembered, however, that it is tempting to diagnose stomal ulceration in a patient who bleeds and has had a previous gastro-jejunostomy. In three such patients the diagnosis of lesser curve gastric ulcer was made with the gastroscope, having been missed radiologically.

BILLROTH I GROUP

TABLE VII

Anastomotic Ulcer. Billroth I. 8

Original lesions. D.U.5. G.U.3

PRESENTATION

Pain	7
Haemorrhage	3

Epigastric pain was the rule and it frequently radiated into the back at the same level. There was often a good deal of delay before the diagnosis of anastomotic ulcer was considered in these patients.

Three of the eight patients presented with bleeding, and emergency surgery had to be undertaken in two.

The first man had an emergency Billroth I gastrectomy carried out for bleeding from a duodenal ulcer. The ulcer was removed. At a convalescent home forty days later he had a severe haemorrhage and was transferred back to hospital. A second emergency operation was done. A further duodenal or anastomotic ulcer had developed just distal to the anastomosis. On this occasion his Billroth I gastrectomy was converted to a Polya gastrectomy and the ulcer removed.

The second man is also worthy of note. His duodenal history started over thirty years ago and included a gastro-jejunostomy, a jejuno-jejunostomy, and a Billroth I gastrectomy. These operations were punctuated with periodic pain and ten serious haemorrhages. He was admitted to hospital on account of a further haemorrhage and in view of his obesity and scarred abdomen, conservative treatment was persisted

Fig. 9 (*c*). Showing " tre-foil " type of deformity of the proximal jejunum.

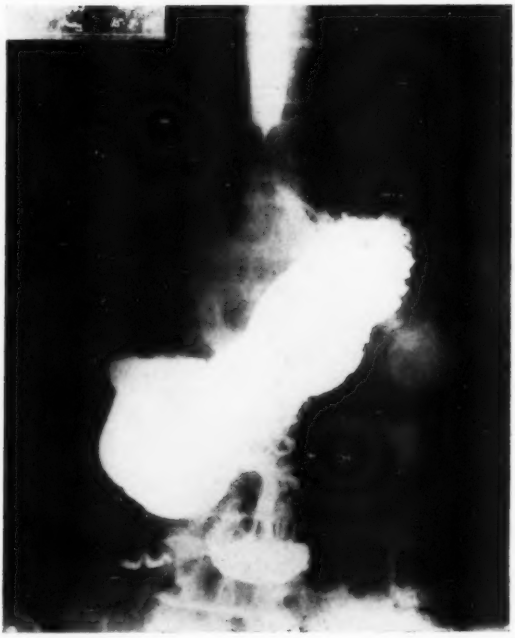

Fig. 9 (*d*). Showing gross deformity of the proximal jejunum.

in to the extent of twenty-two pints of blood, but it was of no avail. His Billroth I gastrectomy had to be changed to a Polya gastrectomy urgently.

The bleeding occurred from an ulcer penetrating the pancreas just distal to the old gastro-duodenal suture line.

Barium meals were done in five patients and a confident diagnosis of anastomotic ulcer was made in four.

Figures 10*a* and *b* are good examples.

It should be remembered, however, that irregularities on the re-fashioned lesser curvatures of Billroth I gastrectomies can be wrongly diagnosed as anastomotic ulcers and to base the diagnosis on radiology alone in such cases will lead to fruitless laparotomy.

Gastroscopy was done in five patients and the only one in which an ulcer was seen is of considerable interest: a man whose history extended over thirty years and included countless haemorrhages, fourteen of which needed admission to hospital. At first he had a duodenal ulcer treated by gastro-enterostomy, and later by Billroth I gastrectomy, but his bleeding continued. The noting of an enlarged spleen " threw a spanner in the works " for a diagnosis, and numerous barium meal studies did not help.

Gastroscopy carried out in a cottage hospital showed the cause of bleeding to be a small ulcer just distal to the old suture line, and what had proved a baffling case in diagnosis for the past fifteen years had at last been solved by the gastroscope, which does not usually help in such cases.

THE GASTRO-JEJUNO-COLIC GROUP

TABLE VIII

Anastomotic Ulcer. Gastro-Jejuno-Colic. 5

PRESENTATION

Diarrhoea	5
Weight loss	2
Faecal vomiting	2

Radiology

In only one of these patients was the diagnosis not made by carrying out a barium enema. Strange as it may seem, if the diagnosis is sought by means of a barium meal, it may be overlooked.

Fig. 10 (*a*). Billroth I gastrectomy with ulcer on anastomotic line. Crater of ulcer seen in profile on lesser curve.

Fig. 10 (*b*). Billroth I gastrectomy with ulcer on anastomotic line. Circular crater of posterior ulcer with radiating mucosal folds.

If neither a barium enema nor a barium meal demonstrates a fistula and one is suspected, it is attractive to believe that a methylene blue enema followed by gastroscopy will give the answer.

The patient who died was tired of life and tired of his surgeons. Three previous gastric operations had failed to convince him that yet another would help, and, refusing operation, his gastro-jejuno-colic fistula was found at post-mortem.

Lastly, there is a group of patients numbering thirteen, in whom no anastomotic ulcer was found at laparotomy. What have we learned from these patients?

Three of them gave a clue to their true nature at gastroscopy, before laparotomy. They were found to have non-absorbable suture material hanging into the lumen of the stomach, a relic of previous surgery, and a warning not to use this material in this situation. At laparotomy this suture material was found to arise from a granulating tract in the stomach wall. Its removal cured the patients.

If the signs and symptoms of an anastomotic ulcer come on in a patient who has done well following his operation and has had few post-gastrectomy symptoms, the diagnosis is usually easy. But where there are many symptoms, it is advisable to hold on till a sign appears. Especially if the patient has never admitted happiness since his gastrectomy. We have had three such patients.

In doubtful cases the bleeding episode should always be verified—one patient who had a useless operation subsequently turned out to be a false witness. His address of 1 Princes Street, Edinburgh, should have alerted our suspicions.

If the pain is little relieved by bed rest, be on the *qui vive*. Anaemia which follows a gastric operation, especially in a woman, is more likely to be due to iron deficiency than to haemorrhage.

Diarrhoea, if it is the main symptom, is a dangerous one on which to base a diagnosis of stomal ulceration. It has disappointed us on two occasions.

Polya group

TREATMENT

TABLE IX

Anastomotic Ulcer. Polya Group. 40

TREATMENT

Vagotomy	17
Vagotomy + revision gastrectomy	7
Vagotomy + excision of ulcer	7
Vagotomy + revision gastrectomy and antrectomy	2
Revision gastrectomy (previous vagotomy)	2
Vagotomy + Polya → Billroth I	2
Mild symptoms	1
Refused surgery	1
Died without surgery	1

Table IX may look complicated—but through the first six groups (thirty-seven patients) runs vagotomy—alone or with removal of the ulcer, or with modification of the gastrectomy.

Naturally, many of these patients have not been followed up for a long time, as this series only started eight years ago.

There are three known patients with further recurrences, all in the group in which vagotomy alone was done. One, a lady, has had her ulcer excised in another country, the second has had a small melaena and no symptoms, and is content to carry on. He has been otherwise well for five years. A third was unhappy on account of bilious vomiting and three years following his vagotomy his Polya gastrectomy was converted to a Billroth I, and now I am afraid he has a further ulcer. A fourth recurrence is possible. It is in the group where vagotomy was accompanied by excision of the ulcer.

The patient who died before he could be made fit for surgery must give us pause. A man aged forty-five, he had his partial gastrectomy for a peptic ulcer four years earlier; since then he had become progressively weaker. Although a man, he was sent to a mental hospital with the diagnosis of anorexia nervosa. He was markedly wasted, with hypo-

tension, and intermittent abdominal pain and distension (Fig. 11*a*). An attempt was made to make him fit for surgery but he died. Autopsy revealed an anastomotic ulcer which had caused stenosis of the gastric stoma with enormous distension of the afferent loop which filled the entire abdomen (Fig. 11*b*).

Fig. 11 (*a*). End result of anastomotic ulcer obstructing afferent loop.

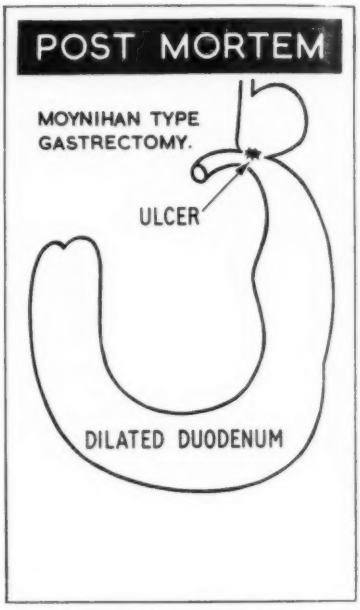

Fig. 11 (*b*). Explanation.

Gastro-enterostomy group

TABLE X

Anastomotic Ulcer. Gastro-Enterostomy. 34

TREATMENT

Dismantle + Polya gastrectomy	28
Dismantle + Polya gastrectomy + vagotomy	3
Vagotomy	1
Found at P.M.	1
Conservative treatment	1

You will see that nearly all these patients were treated by dismantling of the gastro-jejunostomy and performance of a Polya gastrectomy.

There have been three recurrent ulcers in this group and this fact alone has led us to decide that dismantling, coupled with an adequate Polya gastrectomy plus vagotomy, is probably the best operation. It must be remembered, however, that dismantling is often a long and tedious opera-

tion and to add vagotomy to it in every case may well lead to increased mortality.

The patient treated by vagotomy alone is exceptional. He had a short circuit done in 1911 when aged twelve, by Mr. Carless. Thirty-nine years later, we were unwilling to diminish the size of his stomach, thinking that vagotomy alone would suffice, and so far this has been true for the past eight years.

Billroth I group

TABLE XI

Anastomotic Ulcer. Billroth I. 8

TREATMENT

Resection of ulcer + vagotomy	4
Billroth I → Polya (emergency)	2
Billroth I → Polya + vagotomy	1
Vagotomy + pyloroplasty	1

Once an anastomotic ulcer has occurred following a Billroth I gastrectomy for gastric ulcer, there is no doubt that a Polya gastrectomy should be carried out, for anastomotic ulcer following this operation when it is done for gastric ulcer is a pathological curiosity; very few cases have been described. If there is such a thing as gastro-enterological doctrine, this is part of it. It might almost be regarded as a surgical axiom. The tragedy of not realising this is very clearly shown in one patient.

His first operation was a Billroth I gastrectomy for a lesser curve gastric ulcer. Three years later he developed a stomal ulcer, this ulcer was adherent to the common bile duct in which a T-tube was placed at the end of the operation for safety. The ulcer was resected, a vagotomy done and the gastro-duodenal anastomosis reconstituted. Two years later he was admitted to another hospital with a severe haemorrhage which did not respond to blood transfusion. At operation he was found to have another anastomotic ulcer involving his gastro-duodenal artery, and he died following a long operation in which his Billroth I gastrectomy was converted into a Polya gastrectomy, the right operation only two years too late.

Gastro-jejuno-colic group

TABLE XII

Anastomotic Ulcer. Gastro-Jejuno-Colic. 5

TREATMENT

"Triple resection"	2
Colostomy Dismantle + repair colon and jejunum Polya gastrectomy Closure colostomy	1
Dismantle + repair colon and jejunum Polya gastrectomy	1
Refused surgery	1

The advent of the antibiotics which sterilize the large intestine has modified all colon surgery and gastro-jejuno-colic fistula is no exception. The concept of triple resection is neat and appeals to the surgical technician

who is keen to obtain a pathological trophy. But it must seldom now be necessary. The colon and jejunum can usually be repaired and even an emaciated patient can be given a short trial on these drugs in an attempt to control the diarrhoea before being given a temporary colostomy.

Technical considerations

In dismantling, if one keeps exactly to the old anastomotic line, it is often surprisingly avascular.

To repair rather than resect should be the aim. It is safer and simpler in most patients, and we have been able to do it in thirty-two out of forty-eight cases. It may not look elegant but it is immediately serviceable for the biliary and pancreatic juices which it has to carry. With resection there is a potential " closed loop " between the duodenal stump and the end-to-end anastomosis.

In patients where it is difficult to decide whether there is an ulcer or not, there is usually a sentinel gland in the mesentery of the jejunum taking part in the anastomosis.

If vagotomy is planned, it should be done at the beginning of the operation—to be convinced of this, one need only watch the oscillations of an E.C.G. machine attached to your patient when the vagus nerves are being pulled. To subject the heart to this treatment at the end of what may be a long operation is doubtful practice.

If the ulcer is obvious and large, it is better to treat the patient by preliminary bed rest, converting the necrotic tissue into fibrotic tissue with safer suturing.

Sometimes on opening the abdomen, these operations seem to be impossible, but if one works away quietly at the part of the operation which is possible, the puzzle usually solves itself satisfactorily.

In the one patient who died following these operations, the immediate cause of death was found to be acute pancreatitis and his anastomotic ulcer was found to be an ulcer cancer.

FOLLOW-UP

TABLE XIII

Anastomotic Ulcer

FOLLOW-UP

RECURRENCES

Groups	Total	Definite	Possible	Untraced
Polya	40	3	1	4
G.-E.	34	4	—	3
Billroth I	8	1 (dd)	1	—
G.-J.-C.	5	1	—	—

This summarises the present follow-up position. It shows a recurrence rate of over 10 per cent. in a group of patients treated in many different ways and doubtless a rate which can be improved upon when only what are considered the best methods are used.

ACKNOWLEDGMENTS

Before concluding, I would like to thank Dr. Norris, my medical colleague, who has generously allowed me to see and treat so many of his patients; and Mr. Strange, constant companion in all the decisions we have made.

CONCLUSION

If I had an anastomotic ulcer, what would I do? I would seek admission to a gastric unit where a careful gastric history was taken—remembering that gastric patients usually need forty-minute history-taking as opposed to four-minute physical examination. I would like to be in a ward where the BED-SIDE as opposed to the BED-END manner was practised. I would like to be looked upon, not as an awkward problem,

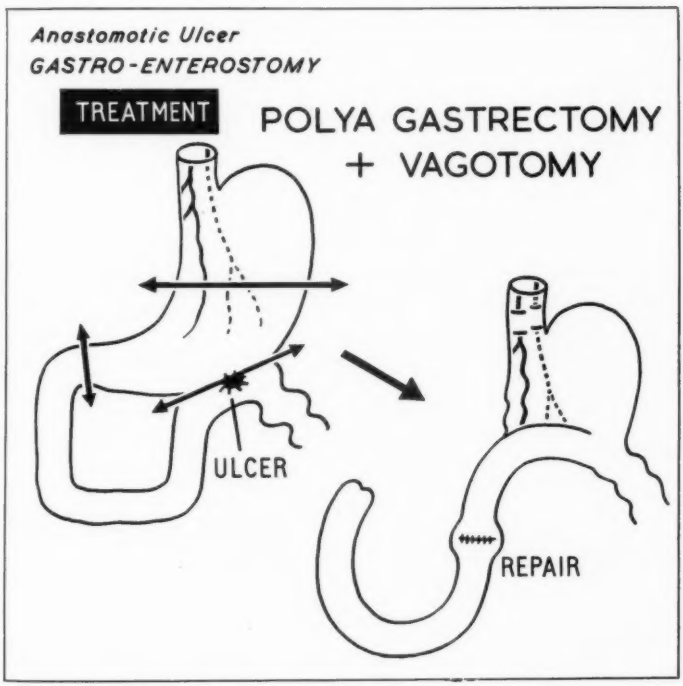

Fig. 12 (*a*). Treatment of anastomotic ulcer associated with gastro-enterostomy.

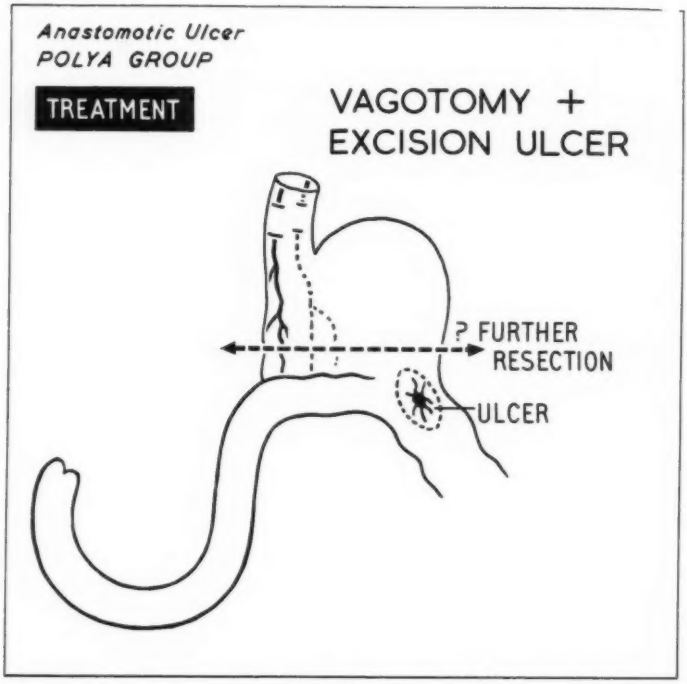

Fig. 12 (*b*). Treatment of anastomotic ulcer associated with Polya gastrectomy.

but as an opportunity for early diagnosis and treatment. I would like to feel that the House Surgeon would write at once to the previous hospital where I was a patient and get accurate details of my past operations. I would like a barium meal carried out by a radiologist skilled and interested in such examinations and working in harmony with the surgeon in charge of my case. I would hope my investigations would go ahead quickly—for often these ulcers are small and heal rapidly. Above all, I would like to feel my surgeon had made a pre-operative diagnosis.

At operation—if I had a previous short circuit—I would like it to be dismantled and converted to a Polya gastrectomy with a vagotomy done at the same time—assuming I was fit enough to stand all three procedures at once (Fig. 12*a*). I would like the vagotomy to be no grovel in the dark, but a clear demonstration of both vagus nerves and their branches by the surgeon to his assistants. I would like him to resect at least 3cm. of each nerve.

If my anastomotic ulcer followed a Polya gastrectomy, I would expect my surgeon to excise the ulcer and perform a vagotomy—or if the gastric

pouch was bigger than the palm of my hand, I would like a higher gastrectomy with the vagotomy.

If my ulcer followed a Billroth I resection for gastric ulcer, I would like it converted to a Polya.

You can see from this how important a weapon vagotomy has become.

Sir Heneage Ogilvie said in 1952: "I believe vagotomy to be dead but not yet safely buried. Fifteen years ago it shot up like a rocket into the gastro-enterological sky; it blazed into a cluster of stars and we all said, 'Oh!' Then the stars died . . ." Surely this rocket has become a satellite, revolving in an orbit of constant usefulness. At least this is the conclusion drawn from these patients.

If anastomotic ulcer is the rogue elephant among our peptic ulcer patients, vagotomy has become our chief weapon in its combat. There are many things we do not understand as yet.

If vagotomy is so important, how can we be certain of its completeness? The lack of completeness may account for many of our bad results, the work of Harold Burge may well throw light on this problem. Does the vagus nerve obey the "all or none" law? Will an unsectioned fibril produce a maximum response from the stomach? Why does anastomotic ulcer follow Polya gastrectomy so quickly and gastro-enterostomy so slowly?

Is it fair to compare the results of operations done in great numbers thirty years ago—in perhaps a more leisurely age—with the results of an operation practised to-day in an age of greater tension?

So far we have found it unnecessary to resect the whole stomach for anastomotic ulcer.

Fig. 13 (*a*). Sir David Wilkie.

Fig. 13 (*b*). Sir James Walton.

Fig. 13 (*c*). Mr. Cecil Joll.

Fig. 13 (*d*). Mr. James Sherren.

These patients particularly need individual thought and care. They have had surgery and failure. They may need to have their confidence re-won. There may be other factors in their lives which need to be dealt with radically. It will not be necessary to do higher and higher gastrectomies, and even total gastrectomy if we are willing to accept responsibility for other obvious ulcer-producing factors in their lives, habits and environment.

In going through the histories of these patients, I took no little delight in discovering that their original operations had been done by men such as Sir David Wilkie, Sir James Walton, Cecil Joll and James Sherren (Fig. 13).

They gave their patients the best they could offer in their day. In the late thirties Sir James Walton started gradually to do Polya gastrectomies for these duodenal ulcers which were accompanied by hypertrophic gastric mucosa as seen through Harman Taylor's gastroscope.

It gives us great encouragement to know that time has modified the views of these surgical giants of the past, but also humility for time will doubtless alter our own most cherished convictions.

VOLUNTARY ANNUAL SUBSCRIPTIONS

THE FOLLOWING FELLOWS have generously undertaken to make voluntary annual subscriptions under Covenant for seven years: T. Berrill, G. Black, R. C. F. Catterall, H. Chitty, H. G. Dain, I. Fraser, P. H. R. Ghey, R. G. Gilbert, L. R. Hutchinson, H. Jackson, A. Lister, J. P. F. Lloyd, R. I. Lloyd, E. MacLellan, A. D. Marston, J. H. Mayer, R. W. Raven, M. J. Roper-Hall, J. C. Scott, E. E. T. Taylor, E. D. Telford, T. M. Thomas, and A. G. Williams.

MALIGNANT EPITHELIAL TUMOURS IN THE SUDANESE

Hunterian Lecture delivered at the Royal College of Surgeons of England
on
13th March 1958
by

B. Brendan Hickey, T.D., M.Ch., F.R.C.S.
Consultant Surgeon, Glantawe Group Hospitals*

IN THE ACCOUNTS of the work of John Hunter, after whom these lectures are named, and to whose memory we are privileged to pay tribute, it would appear that his experience of disease arising outside the United Kingdom was small, as could only be expected in the eighteenth century. John Hunter travelled as did many modern surgeons in a military capacity being stationed in Bell Isle and then Portugal. While he learnt much about treating wounds, he spent part of the time of inaction inseparable from war service in study of the natural history and physiology of the native fauna. He also criticised his administrative superiors. We can only speculate on the magnitude of the results that would have been forthcoming, had modern facilities of travel been available to John Hunter. We certainly know that he would have grasped the multitude of opportunities presented.

GEOGRAPHICAL AND ETHNIC NOTES

The Sudan is an area of approximately 950,000 square miles carrying in the region of 12 million inhabitants bordering on Egypt in the north along the 22nd parallel, and 1,200 miles south at the southern extremity, on Uganda. Its peoples are fairly sharply divided into northerners inhabiting the provinces of Dongola, Kassala, Dafur, Khordofan, Blue Nile and Khartoum, and southerners occupying Upper Nile, Bahr El Gazal and Equitoria. The northerners only penetrate the southern provinces in small numbers as traders and administrators.

The northern Sudanese are Arabic speaking Moslems classed as Arabs and are from the Hamitic and Semitic tribes. In the area around and immediately north of Khartoum they are chiefly Nubians, but all are of exceedingly mixed stock. In colour the average northerner is very dark and, though there is a fair range of variation in colour, few could be mistaken for Egyptians. The greatest proportion of the population live in villages and are occupied with various forms of agriculture and herding, chiefly goats and camels. The largest centre of population by far is the three towns, Khartoum, Khartoum North and Omdurman with a total population of about 250,000 and it is here that the few light industries are centred. The only other locations where industry is carried on to any extent are the town of Port Sudan and Atbara, the railway centre. Included among the northern provinces are considerable areas of desert

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inhabited only by Bedouin tribesmen. The climate is hot and dry. Sunlight is intense the major part of the year, and temperatures up to 120deg.F. the rule.

The southerners are a much more primitive people, chiefly pagans and are essentially Negro Nilotic tribes, Shilluks and Dinkas, the latter chiefly living in the Bahr el Gazal province, while the Shilluks occupy the west side of the Nile north of Lake No. Farther south and west of Bahr el Gazal live the Bongas and on the Nile-Congo watershed are found the A Zandes, a numerous people whose tribal areas extend far beyond the Sudan into the French and Belgian Congo and who are distinctly lighter in colour than their neighbours. Apart from a cotton factory at Nzala in Equitoria, there are no industries and there is no large centre of population in the territories. They speak no Arabic, but the relatively few with education speak English.

The health of this mixed populace was at the time of this investigation the responsibility of the Sudan Medical Service and this service provides hospitals and dispensaries throughout the whole country, assisted in parts by Mission Medical Organisations. All major pathological investigations are undertaken in the Stack Laboratories for Medical Research, Khartoum.

MATERIALS AND SOURCES

The material presented consists of specimens of tumours, which have been received in the Stack Laboratories for Medical Research in Khartoum for the period of eighteen years from 1935 to 1954 and comprise 1,337 specimens, all of which have been examined histologically. All of these are primary tumours with the exception of some probable secondary growths found in the abdominal cavity, but arising from abdominal viscera. The large majority are operation specimens as it is most exceptional to obtain permission for post-mortem examinations in this country. The Stack Laboratories receive all the specimens submitted for histological examination in the country and it is considered that they are representative of the indigenous disease picture of the patients admitted to hospitals. The occasional malignant growth submitted from the European patient has been excluded from this investigation. The majority of the specimens we received from the hospitals in the northern provinces.

The histological study has been limited to epithelial growths because experience is that patients with sarcomata, particularly involving the limbs, appear at hospital very late and still very frequently refuse amputation, generally the only possible treatment. Consequently the laboratory records are unrepresentative, and do not accord with clinical experience.

The actual records available in the laboratory are incomplete in that there are only scanty and occasional clinical details available and the ages of the patients are not given, but the older Sudanese has in general only the haziest idea of his age, and their own estimates are often obviously wildly wrong. From hospital experience, it appears though that there is

no gross difference between the age groups of those patients suffering from malignant disease in the Sudan and in England.

The number of growths according to site and numbers are as below in order :

Skin	Comprising : Epitheliomata	284	
	Malignant Melanomata	108	
	Rodent Ulcer	45	
			437
Breast			306
Uterus			91
Rectum and Anus	Comprising : Adenocarcinomata of Rectum ..	44	
	Squamous Carcinoma Anal Canal ..	22	
	Melanoma of Anal Canal	1	
			67
Salivary Glands ..	Comprising : " Mixed "	47	
	Carcinoma	9	
			56
Bladder			54
Mouth, including Lips			51
Abdominal			45
Vagina			38
Liver			38
Penis			26
Ovary			23
Thyroid			19
Prostate			18
Jaw (adamantinomata)			17
Testis			16
Tongue			7
Intestine (Colon)			7
Kidney			6
Vulva			5
Stomach			5
Spinal Cord (Glioblastoma Multiforme)			1
Oesophagus			1
TOTAL			1,337

It will be seen that the commonest site for malignant growths is the skin, followed closely by the breast which produces the most frequent single growth, with the female genital tract third. This corresponds generally with the findings of other investigators in Africa, Elms and Baldwin (1947) in Nigerians, and Vint (1935) in natives of Kenya, who all find skin cancers ranking high with breast and female genitalia approaching. In the adjacent country, Uganda, Davies (1948) is of the opinion that while skin cancer is not so frequently seen in post-mortem material, it is actually the commonest malignant tumour among central Africans.

CUTANEOUS NEOPLASMS

Epitheliomata

The high frequency of cutaneous carcinomata among the inhabitants of the African continent has been commented on by most investigators in this field. Vint, Kenya, loc. cit., Elms and Baldwin, Nigeria, loc. cit., Geyer (1947), Dakar, Gelfand (1949), Southern Rhodesia, rate among

them the commonest malignant tumours in the areas investigated. These findings are of considerable significance when compared with similar records concerning American Negroes. Steiner (1954) has reviewed the literature and added his own investigations from Los Angeles Ho Of 135 cases of cutaneous epitheliomata at Los Angeles Hospital, occurred in Caucasoids, thirteen in Mexicans and only one in a Ne It is apparent that the American Negro is much less liable to skin ca. cinomata than his white counterpart, and skin carcinoma occupies a very low place among the cancers he is liable to.

Analysis of the site of the cutaneous cancers in Sudanese throws further light on these differences. The site distribution of 284 growths is as below:

Leg	80
Face	78
Arm and Hand	29
Scalp	26
Foot	14
Buttock	8
Back	1
Unspecified	48
	284

Steiner loc. cit. in a comparable series of 135 skin tumours seen in Los Angeles quotes this site distribution:

Head and Neck	97
Upper Extremities	16
Trunk	14
Lower Extremities	8

The great preponderance of tumours of the leg among the Sudanese is at once apparent. The picture is in keeping with the other analysed African figures and also Ceylon where Cooray (1944) found 61 per cent. of the skin cancers arose from the lower extremity and he attributed this to the prevalence of chronic ulcers as did Denoix (1947) who records a high incidence of epitheliomata and ulcers in French West Africa. It is suggested that among the Sudanese this preponderance is due to trauma and the frequency of chronic ulceration of the type known generally as tropical ulcer of the shins. Varicose and gravitational ulceration as seen in Europeans happens rarely in the Sudanese, but chronic lymphatic obstruction, probably due to filariasis, accounts for a few more ulcers. The foot and leg of the majority of men when working are bare and constantly exposed to thorn pricks and cuts and bruises from sharp stones. The shin is particularly exposed, it being rare to see a Sudanese working man without scarring in this region, with or without ulceration, and it appears that these growths arise in either ulcers or the unstable scars left when they heal.

The possible contribution of sunlight in the aetiology of these tumours may be considered. If we exclude the growths of the lower extremity the site distribution in the Sudanese is proportionately the same as in Steiner's

figures. Though it has been strongly suggested by Schreck (1944 *a*) that the Negro in America is largely protected from developing cutaneous carcinoma of solar origin by his pigment, here in the Sudan, particularly north from where most of the specimens come, the sun is of remarkable intensity and from their site on exposed parts, apart from the lower extremities, it appears probable that these growths are largely solar induced.

The lack of growths arising on the trunk is probably of significance, for even the poorest northern Sudanese usually works with his body covered and the sole epithelioma of the back was seen in an old boatman who had pulled ropes over his shoulder for many years and it arose in the cornified track made by these ropes. In this regard, it may be noted that Schreck (1944 *b*) finds that in white and coloured people of America the incidence of epitheliomata on the non-exposed parts of the body is identical.

Histology

These tumours were chiefly cornified growths, the degree of cornification of the growths of the lower extremity being remarkable.

Clinical course

In general the growth seems to be of low malignancy particularly when it occurs on the leg. The patients present with enormous fungating growths which they have treated for years, but metastasis to the regional glands are exceptional and general dissemination is not recorded.

MALIGNANT MELANOMATA

The frequency of malignant melanomata in the Sudan has already been indicated by Hewer (1935) and in all records it appears that in the African living in the tropics this is a relatively frequent growth. The site distribution of the growths is as below :

Foot	91
Leg	10
Arm and Hand	6
Anus	1
	108

The other investigators in Africa already quoted and in addition Enos and Holmes (1951) from Panama find that the tumour occurs much more frequently on the sole of the foot.

It is generally agreed that under tropical conditions there must be an additional factor which must account for the frequency of these growths among coloured people. Morris and Horn (1951), in the United States, find that malignant melanomata are between two and four times commoner in the white man than the Negro. From American investigations it does appear that the coloured races have a greater inherent tendency to develop growths on the foot, Meuling and Burdette (1950) finding 50 per cent. arising on the foot in these races.

The aetiology of these growths is debatable. It is known that among Europeans up to 61 per cent. arise in pre-existing moles (Ackerman, 1948). Hewer, loc. cit., suggests that they arise in the naevi which he had shown are of frequent occurrence even in the darkest Sudanese. At first sight it would appear that this would not explain their origin from the sole of the foot as on microscopic examination this area is free from naevi, an observation also made by Cooray loc. cit. However, on examination of the sections, while in the large majority there is no clue as to their origin, in four growths on the sole of the foot, Figs. 1, 2, 3 and 4, the melanoma did appear to be developing in the region of a naevus and it is suggested that Hewer's hypothesis may be correct, but the original naevus is small and hidden by thick epidermis.

It has been suggested, perhaps originally by Eve (1903), that trauma is the exciting cause of the malignant change. Certainly the foot of the Sudanese is particularly exposed to mechanical trauma, in particular sharp stones and thorns, and physical in the form of the intense heat of the ground, and it is considered reasonable to conclude that these agents must be factors here. It is admitted that a clear history of trauma cannot be obtained from patients, and Wright, Clark and Milne (1953), finding only 4·5 per cent. of British patients give such a history, question its role, but here it is difficult to find any other possible factor, and Wright (1949), is of the opinion that trauma accounts for the relative frequency of the growth on the foot among Europeans.

The impression that malignant melanomata of the foot are relatively benign, as suggested by Hewer in the Sudan and Enos and Holmes loc. cit.

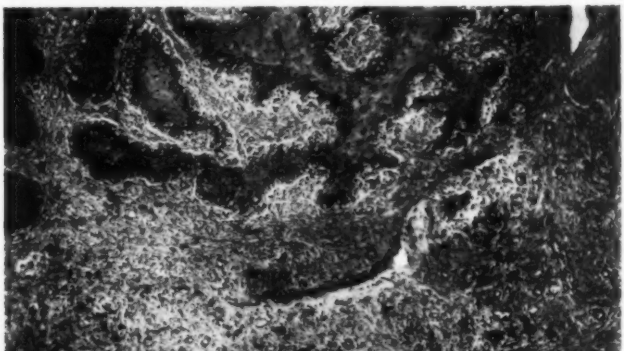

Fig. 1. Malignant melanoma arising among naevoid cells in sole of foot ×56.

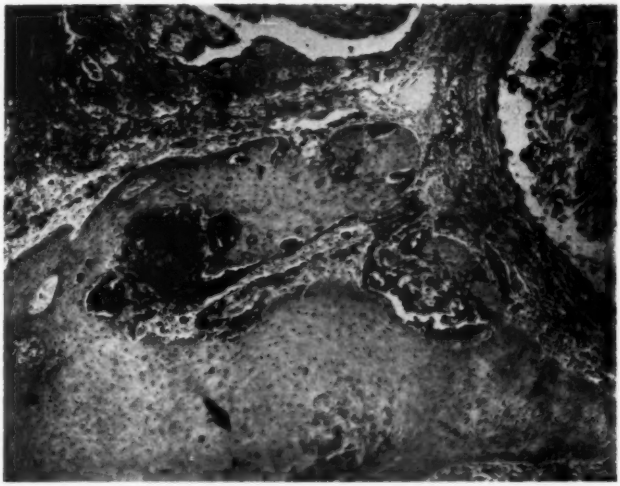

Fig. 2. Nest of frank melanoma malignum lying in the thick epidermis of sole of foot with adjacent naevoid cells ×56.

in Panama, is well confirmed clinically. Metastasis is to the inguinal and neighbouring lymph nodes occurring up to three to four years after the appearance of the primary growth, while we have had no example of general dissemination in Khartoum or Omdurman hospitals during the three years 1952-55.

Histology

Immense variation in the amount of pigment was noted. The darker specimens were so heavily pigmented that cell structure could hardly be distinguished. Rough classification into heavy, moderate and light revealed :

Heavy	23
Moderate	37
Light	45
Absent	1

The most notable feature was paucity of pigment in many specimens which appeared amelanotic, only very careful scrutiny revealing a few scattered pigment cells.

The cell types were investigated on the basis of the classification of Dawson (1925) with these results :

Predominant Cell Form	
Round	19
Polyhedral	41
Spindle	46

Pleomorphism was definitely uncommon and never sufficient to leave any doubt as to the predominant cell type. There is no evidence that the histology of the malignant melanoma in Sudanese differs from other races. This observation is in accord with those of Anderson (1941) and Bishop (1932) who find no difference between the morphology of the malignant melanoma seen in the Negro and the Caucasoid.

Rodent ulcer

The finding of forty-five rodent ulcers in this series is perhaps surprising, for farther south in Africa, Vint loc. cit., and Smith and Elms (1934), comment on its rarity. The condition would appear to be met with oftener in the north of the continent, as Dolbey and Mooro (1924) report on its frequent occurrence in Egypt.

The site distribution as far as could be ascertained is as below :

Face	18
Eyelid	7
Scalp	3
Temple	2
Forehead	2
Anus	2
Abdominal Wall	1
Toe	1
Penis	1

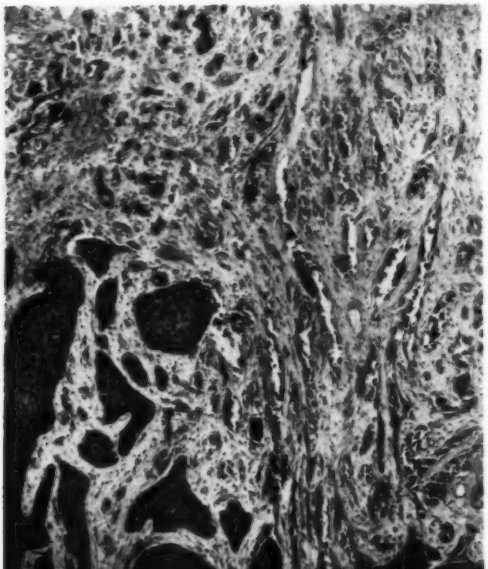

Fig. 3. Naevoid and melanotic cells from sole of foot ×56.

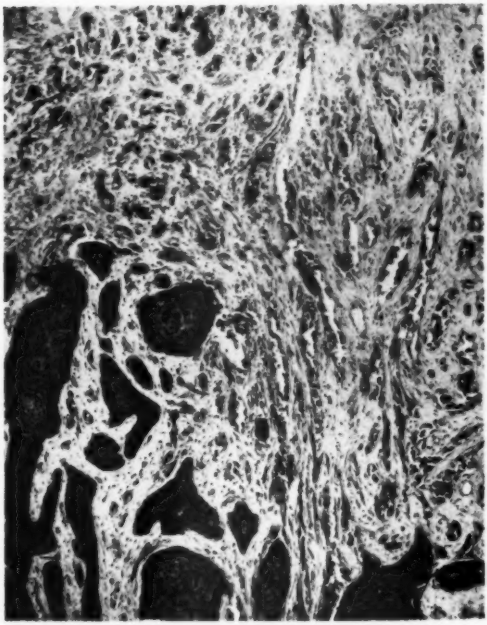

Fig. 4. Scattered naevus cells with malignant areas from sole of foot × 56.

This distribution is similar to that found among Europeans, Willis (1953), in that the parts most exposed to the sun are most commonly affected and it is reasonable to suppose that the growths are likewise induced by the same agent, most probably actinic rays, among the Sudanese.

Relation of maduramycosis to cutaneous carcinomata

Maduramycosis is one of the commonest surgical conditions in the Northern Sudan (Abbott 1956). It is characterised by extreme chronicity and the development of multiple sinuses discharging pus and granules of fungus which heal and re-open over a period of years. Bone destruction and secondary infection is the rule and the occasional appearance of an epitheliomata in one of the sinuses could be reasonably expected, but there is no record of the two conditions being seen in the same specimen.

BREAST

This cancer, providing 306 specimens, is the commonest single cancer seen in our laboratories. Considering the local conditions it is almost certain that it must be the commonest in the Sudan, for the women are considerably more reluctant to enter hospital than the men. Cancer of the breast

ranks high in all the African series already quoted, but is not in the first place in any other. The reason for this is not apparent and it may well be that in actual fact this figure is fortuitous, but there can be no doubt but that the tumour is very frequent. However, in the year by year analysis, the breast cancers retain first place even in the earlier years where total numbers were small.

Sex distribution

There were four definitely recorded carcinomata of the male breast, which is in accord with the usual male to female ratio for this growth. We have no evidence that carcinoma of the breast is significantly commoner in the Sudanese male than the European.

Parity and lactation

No particulars are available, but the unmarried Sudanese woman is a very rare exception and the large majority have borne children, and in these, lactation is carried on for years, their children being breast fed until the age of three or even over. Sterility in the married woman is not uncommon, but there is no reliable method of finding its real incidence, and it is not possible to ascertain whether parity and lactation conveys any relative immunity in the Sudanese woman.

Age

Note has been made of the unreliability of the patients' statement of age, but from hospital experience one can state with certainty that the majority are women of menopausal age. Unfortunately most come to hospital late and fungation is common. The clinical course of the disease appeared much the same as in the European.

Pathological types

All varieties are encountered with the exception of mastitis carcinomatosis. There are, however, no Paget's disease of the nipple recorded and only one specimen from a Sudanese has reached the Stack Laboratories which was in a male recorded by Archibald in 1942.

Investigation of the specimen demonstrated very great variation in the histology of individual sections, and histological classification was considered to be valueless.

Aetiological Implications

The true aetiology of breast cancer being unknown, it is not possible to make even tentative deductions, though it can be said that the breast of the Sudanese woman is certainly susceptible to cancer, that it is subject to the same physiological stresses as the breast in other races, and that it frequently becomes carcinomatous.

UTERUS

Ninety-one examples of uterine carcinomata constitute a sizeable proportion of growths, and it is certain that taking into consideration

the reluctance of the women to enter hospital, this must be a common disease. In other parts of Africa, however, there appear to be considerable variations in frequency. Berman (1935) and Higginson (1951) found it to be the commonest tumour in the Bantu, the latter finding it comprised 24 per cent. of histologically diagnosed neoplasm and 54 per cent. of carcinomata in females and at the other end of the scale Vint (1935) in Kenya, found only one of carcinoma, but two of chorion epithelioma in 546 native tumours. In the main, the majority of investigators in Africa have found uterine cancer to be common, and the gross variations are probably due to selection of some sort. In the United States, the relative frequency between negro and white has been studied extensively, and the general conclusion (Steiner, 1954) is that carcinoma of the uterus is certainly as common, if not commoner, in the negro as compared with the white woman.

The proportion of cervical to corporeal growths is approximately two cervical to one cancer of the body. It is probable that a number which were diagnosed as vaginal growths are actually extensions from the cervix. The proportion is approximately similar to British figures, Kimbell (1954) recording a two to one proportion from England and Wales during the five years ending in 1952. The only African figures available are those of Berman (1935) who in the Bantus found twenty-five cervical and fifteen of the body in a series of forty cases. Randall (1945) suggests that the cancer of the body becomes more frequent with advancing age, but with the details available it is not possible to find any such trend among the Sudanese.

Histology

Of the carcinomata of the corpus 90 per cent. were adenocarcinomata and 10 per cent. squamous. No chorion carcinoma was found, though more recently two cases have been recorded.

It may be noted that to date no endometrioma has been recorded in the Sudan.

Aetiological implications

Uterine carcinoma occurs commonly in the Sudanese woman, and, in general features, the disease resembles that seen in the European and it is reasonable to conclude that the same basic factors cause the growth. If we can accept Steiner's general conclusion that the African living under similar conditions to the Caucasoid is equally liable to develop uterine carcinoma, a more detailed study might disclose further aetiological factors in the Sudanese, for the male Mohammedan is circumcised at about puberty (we have the evidence of Nath and Grewal (1935) that the Muslim women in India are less liable to carcinoma of the cervix than the Hindu), but in addition the Northern Sudanese woman herself is almost always circumcised at about the age of five.

RECTUM AND ANAL CANAL

These growths are of considerable frequency in Sudanese as compared with most other African statistics reviewed by Steiner, who notes the considerable variation in their incidence with figures as low as two in 562 in Kenya (Vint). In a neighbouring country, Egypt, Dolbey and Mooro (1924) found only seven cancers of the rectum in 671 cases of malignant disease and Greiss (1948), fifty-six in 1,658 cancer specimens. Clinical impression in the Sudan is that the disease is rather commoner than these statistics show.

A relative frequency of squamous growths of the anal canal which is half as common as adenocarcinoma of the rectum is remarkable. These growths of the anal canal are not infrequently seen in the wards and out-patients departments, and always seem to be advanced. Rapid lateral spread and gross secondary infection with sinus formation is the rule. No reason for this can be deduced apart from the fact that the Sudanese is undoubtedly prone to non-specific granulomatous conditions around the anus and these might be precursors of squamous celled growths.

It might be expected in this country that where bilharzial infection occurs that infestation is a factor in the aetiology of rectal growths, but in only one adenocarcinoma of the rectum could the parasite be seen. Dolbey and Mooro, loc. cit., came to the conclusion that bilharzial infestation was not a factor in causation of carcinoma of the rectum in Egypt. There is no known record of familial intestinal polyposis in the Sudan.

Adenocarcinomata

There was very considerable variation in the histological picture. The commonest growth was an adenocarcinoma as seen in the table below:

Adenocarcinoma	55 per cent.
Anaplastic pleomorphic carcinoma	21 per cent.
Colloid carcinoma	15 per cent.
Malignant polyp	9 per cent.

Of all these growths 27 per cent. showed downward spread into the wall of the anal canal. The actual figure is probably a lot higher. It is most probably an expression of the late stage at which these growths are generally seen.

Squamous epitheliomata

Here again there is considerable variation from cornified growths to those showing a degree of anaplasia rather remarkable for growths of epidermal origin. The anaplastic growths numbered four. Spread, so far as could be ascertained, was chiefly in a lateral direction, only two extending demonstrably upwards as far as the rectum.

SALIVARY GLAND TUMOURS

The " mixed " type are included among malignant epithelial tumours because of their undoubted tendency to infiltrate locally and recur. In all the African series summarised by Steiner they occupy prominent

positions, and the Sudan appears to be no exception ; that their relative accessibility contributes a falsifying factor has been suggested, but here the equally accessible tumours of the mouth and lips rank somewhat below the salivary tumours, suggesting that the relative frequency is real. A similar observation is made by Gelfand, loc. cit., in the Bantu of Southern Rhodesia. The writer (1957) from a smaller Sudanese series finds that their distributional frequency between the main salivary glands and other sites is similar in the Sudan to other parts of the world, viz., about 80 per cent. in the major glands and 10 per cent. distributed in minor glands and 10 per cent. in the palate.

The proportion of histologically malignant growths is nine to forty-seven, approximately 16 per cent., while Janes (1957) found in Toronto eighty-nine carcinamatous growths to 203 adenomatous, 33 per cent. in very much higher proportion. Comparison of these two series is fraught with possible fallacies, but one comment may be made, and that is that the proportion of malignant growths may be artificially low in the Sudan because one would expect to receive a considerable number of these in an already inoperable state, and they would not contribute to the biopsy material.

BLADDER

It is apparent that carcinoma of the bladder is fairly common in the Sudan and it might be expected that Schistosoma haematobium, which is endemic in some areas, might be the cause as in Egypt, where both bladder cancer and bilharziasis are very common; in fact, bladder cancer is, according to Makar (1957), the commonest growth seen in some hospitals. However, in only 5.9 per cent. of the sections were ova discovered. This apparently small proportion of bilharzial bladder cancers may be commented upon. First it should be noted that Willis (1953) and also Price (1940) have thrown some doubt on the accepted theory that the schistosome is a causal agent, though Makar's observations are difficult to explain on any other basis. Secondly, the actual infested areas, the cotton growing parts, are three : the Ghazera, Gish and Zeidab, important economically, but small in relation to the rest of the country. Finally, the population is well aware of the symptoms of bilharzial urinary infestation and report early for treatment. Advanced cases with calcification of the urinary tract are very rarely seen.

Vesical calculi are frequent in spite of statements to the contrary (Aird, 1949), but there is no evidence of these being contributory, and there are no industrial hazards likely to cause bladder growths.

Histology

The type distribution is as below :

Squamous celled	47 per cent.
Transitional celled	41.2 per cent.
Malignant papilloma	11.8 per cent.

The proportion of squamous growths is high and there is no apparent reason for this. Hollands (1952) records only 11 per cent. squamous carcinomata among 227 malignant bladder growths in England.

BUCCAL AND TONGUE CARCINOMATA

It was not possible to subdivide these growths according to site with any accuracy except for the tongue, which is listed separately.

In the main they arise from the inner surface of the cheeks, but it is very probable that a number included here have originated in the antrum, and from the gum margins. A number of factors may be present causing these growths, but most probably dental decay, which is very common in the older Sudanese, and the presence of sharp carious teeth stumps universal among most Sudanese, is the most potent. The Sudanese does not chew betel or any similar compound.

Leucoplakia, syphylitic or otherwise, is rarely seen in the Sudanese and this may account for the few growths of the tongue recorded. Dolbey and Mooro, loc. cit., note that leukoplakia is similarly uncommon in Egypt.

VAGINA AND VULVA

A total of thirty-eight carcinomata of the vagina is remarkable. Willis (1949) states that primary carcinoma of the vagina is a rare disease comprising only 1 per cent. of the cancers of the female genital tract. It is most probable that a proportion of these tumours which are all squamous celled arise from the cervix, for it is notable that the majority have been received in the laboratory in the earlier years. There is one possible additional explanation in the Sudan, as in this country female circumcision is universal in the north and resultant inadequate drainage of the vagina might be a factor.

Per contra carcinoma of the vulva has rarely been found, only five specimens having reached the laboratories, and the destruction by this operation of a large part of the vulva adequately explains this.

PENIS

The twenty-six specimens are largely from Mohammedans, but the majority of races are circumcised in the Sudan, and we have further proof that if the operation of circumcision is delayed beyond infancy, while it may reduce the chances of developing carcinoma of the penis, absolute immunity is not conferred. In India, Nath and Grewal (1935) found the disease occurring in the circumcised Mohammedan, though far less frequently than in the uncircumcised Hindu living under very similar conditions.

THYROID

Primary carcinoma of the thyroid occurs in nineteen cases. Clinical experience suggests that it may well be more common in the Sudan than this figure would suggest. Goitre is seen not infrequently in this country, seventy-four specimens from non-malignant goitres having been received

during the period under review. Woodman (1952) states that there are at least five areas in the country where goitre is endemic, that most fully authenticated being an area centred on Lirangue in Equitoria Province, where 3 per cent. of the total population have been estimated to be affected. Malignant goitre has been noted by Woodman, and he considers that malignancy among the older goitres is not infrequent but quotes no statistical evidence.

Other figures from the African continent show considerable variation. Davies', loc. cit., post-mortem studies in Uganda do not mention the condition, while Vint, loc. cit., in Kenya and Geyer, loc. cit., in French Equatorial Africa record minute percentages. Elms and Baldwin in Nigeria record proportions commensurate with these figures and in Egypt, Dolbey and Mooro, loc. cit., record fifteen out of 671 cases of malignant disease.

PROSTATE

This growth occupies, with eighteen specimens, a low position, and the probability is that it is commoner than laboratory statistics would indicate. All types of prostate carcinoma are seen in the Sudanese and not all, particularly those presenting with skeletal secondaries, are submitted to operation; hence these figures represent only a portion of the growths. During the period under review, sixty benign enlarged prostates came to the laboratory, which would give a proportion of approximately one malignant to three benign glands, but probably the number of non-malignant glands is not a true reflection of their incidence, as Sudanese patients with enlarged prostates often arrive in hospital *in extremis* after repeated unskilful attempts at catheterisation.

For laboratory figures as distinct from post-mortem this series shows a high frequency for Africa, Vint, loc. cit., reporting none among 546 malignant growths in Kenya, Gelfand, loc. cit., one among 344 in Rhodesia and Geyer, loc. cit., one among 170 in Dakar, but African post-mortem studies give the condition prominence; Gelfand (1949) finding they ranked seventh in the tumours found in the Bantu, and Davies (1948) giving carcinoma of the prostate the same rating in Uganda. Although the numbers are not large, eighteen as noted, it is the largest collected native African series reported to date, and it is suggested that this is a measure of the thoroughness with which histological specimens have been collected in the Sudan.

ADAMANTINOMATA

Compared with fifty-one epitheliomata of the mouth and lips sixteen adamantinomata constitute a sizeable proportion of tumours in this region, and, in hospital practice, jaw tumours, often of enormous size, are frequently seen. All the specimens were true adamantinomata arising in the jaws.

Histology

Though all were recognisable, there was considerable variation in

cellularity and amount of matrix. Two showed marked cornification and one of these melanotic cells. Presence of melanotic cells on occasion has been noted previously by Robinson (1937). None of the growths was metastatic.

TESTIS

The testicular tumours are in no way notable. They are evenly divided between seminomata and teratomata.

KIDNEY

This is a small group of only five growths, all clear celled carcinomata. Renal calculi are seen and operated on, but no carcinoma of the epithelium of the renal pelvis is recorded. In view of the fact that these tumours so frequently present with haematuria only and swelling appears late in the disease it is probable that they occur more frequently than this figure would indicate.

They certainly occur in other African races, though they are not common, Uys in the Bantu recording less than 1 per cent. of renal tumours of all kinds in autopsy series of 3,707. Wilms tumour is occasional but it was not possible to ascertain the relative frequency of the two types of growth.

GASTRO-INTESTINAL NEOPLASMS

As compared with any British or American statistics, cancer of the stomach and large intestine are rare. The largest group which may give an indication of their relative infrequency is that of unspecified abdominal carcinomata comprising forty-five, while those gastro-intestinal cancers identified (rectum excluded) form a minute group of seven intestinal and five gastric. The reason for the lack of identity of the primary is that the Sudanese tends to come to hospital rather as a last resort, after treatment by unorthodox practitioners has failed, and, particularly if a tumour is the presenting symptom, it is first seen when big. Hence at laparotomy a search for the primary is generally profitless, and may be dangerous, so the surgeon prefers to take a biopsy only. Further, it is very probable that the group of forty-five unspecified abdominal growths include a number of advanced primary ovarian cancers, even decreasing further the number arising from the gastro-intestinal tract.

Clinical experience in Khartoum and Omdurman hospitals bears out the suggestion that cancers of the gastro-intestinal tract are truly uncommon, for patients do report with acute and chronic gastro-intestinal disturbances and abdominal swellings, but it is entirely exceptional to find carcinoma of the stomach or colon responsible for these. It is difficult to maintain that carcinoma of the colon in particular is missed, for adenocarcinoma of the rectum is recorded in numbers commensurate with growths of the whole of the rest of the gastro-intestinal tract. Further, numerous patients with dysenteric disorders are fully investigated, this including sigmoidoscopy in hospital, and, to the writer's knowledge, only one carcinoma of the colon has been discovered, originally mis-diagnosed

as a dysentery in this way during the past three years in Khartoum Civic Hospital. Acute surgical cases yield very few examples also. Intestinal obstruction is not uncommon, but carcinoma of the colon is a most infrequent cause. Were it usual to perform a laparotomy, it might well be maintained that a number of abdominal growths was missed, but laparotomies are frequently performed, particularly in patients who present with abdominal swellings. The most usual operative finding, however, at all ages, is one or other variety of abdominal tuberculosis. The incidence of carcinoma of the rectum and anal canal has been referred to.

COLON

The rarity of colonic neoplasms is much in accord with other African series; Berman finding them consistently only 2.7 per cent. of all neoplasms in the Bantu, and Elms and Baldwin 1.4 per cent. in West Africa. Davies (1948) gave colonic growths fifth position in Uganda, which appears to be the highest African rating. Turning to the African resident in the United States of America, it is reasonably established from investigations by Steiner (1954) in Los Angeles, and others in America, that the Caucasoid has a greater tendency to develop colonic neoplasms compared with the negroid, and probably other races as well, living under similar conditions.

At first sight, it would appear surprising that among the natives of a tropical country, where inflammatory colonic disorders are so frequent, there should be so few diagnosed colonic neoplasms, and the inference is that the dysenteries do not predispose to development of carcinomata. The most probable precursor of the carcinoma is the polyp so often seen in conjunction with malignant disease, and it is probable that the Sudanese have less tendency to form polyps than the European. I have noted the absence of any known family with multiple polyposis, and neoplastic polypi were not seen in the numerous routine sigmoidoscopies performed.

STOMACH

The small number (five) of recorded gastric cancers has been noted, and it would appear that until present times the Sudanese has been relatively immune to gastric cancer. The causes of cancer of the stomach are not known, but in no African series reported does the growth occupy a high place, Berman (1935) and Higginson (1951) finding it comprised 8.6 per cent. of all malignant tumours and 9.5 per cent. of all tumours of the alimentary tract respectively in the Bantu. Greiss found twenty-six gastric carcinomata in 1,568 cancers in Egypt. Davies (1948) from necropsy material found gastric cancer occupied sixth position in the neighbouring territory of Uganda.

Although the aetiology of cancer of the stomach is, as had been stated, unknown, it does appear that peoples who are not liable to simple gastric ulceration are less liable to develop cancer of the stomach. Price (1928) found that peptic ulcer was seven times more frequent in Koreans than

Chinese and the incidence of gastric cancer ran parallel to ulcer in these peoples. Other similar observations in the Far East were made by Boone (1935-1937), who found no gastric cancer and no gastric ulcer in the Malays of Batavia, while both were frequent in their Chinese and Philippino neighbours. Snijders and Straub (1924) made similar observations on the basis of necropsies in Sumatra.

Among the Sudanese peptic ulceration is an infrequent medical condition, and is confined to duodenal ulceration. In Khartoum and Omdurman's several hospitals, occasional perforated duodenal ulcers are operated upon, but there is no record of a perforated gastric ulcer. Neither are gastric ulcers found in the routine radiological investigations of the intestinal tract, which are quite numerous. It is suggested that the possible absence and certain rarity of gastric ulceration among the Sudanese may be correlated with the rarity of carcinoma of the stomach. The statistics were reviewed by Steiner (1954) and suggest that the African in general, when he has migrated to other countries, becomes liable to gastric carcinoma as frequently as the other inhabitants, and the evidence available suggests that the immunity of the Sudanese is due to environment rather than racial factors. No exact statistics are available as to any increase of peptic ulceration among the Sudanese, but hospital experience suggests that duodenal ulcer is more frequently recognised in the town dwellers and cases of gastric ulcer may arise later. It is possible that this may bring in its train an increase in carcinoma of the stomach.

LUNG

Primary cancer of the lung is not recorded in this series, but it can occur in the Sudanese as two cases have been discovered during the year 1955, though it appears the condition is still of great rarity.

In view of the rarity of post-mortems the validity of this statement could be questioned, but on the positive side it must be recorded that :

1. Physicians in the Sudan have been aware of the occurrence of primary lung growths for as long as they have been in Europe and America, and have always considered its possibility in diagnosing pulmonary conditions. These growths have been diagnosed in Europeans, but not in Sudanese during the period under review.

2. Large chest clinics are established in the towns of Khartoum and Omdurman and full investigation of chest conditions, including bronchoscopy, are undertaken. These have revealed no cases of primary lung cancer during the time under survey.

3. Secondary pulmonary new growths are seen and diagnosed in hospitals and chest clinics.

4. Survey of all sections of growths removed from the chest during the period under review showed no evidence of misdiagnosis.

The possible reasons for this rarity of lung cancer may be considered under these headings :

1. *Atmospheric pollution.* Without analysis of the air, it is entirely safe to say that pollution from motor vehicle fumes is negligible compared with England. The greater density of traffic in the towns of Khartoum and Omdurman hardly reaches that of an English market town. The large majority of vehicles are petrol not diesel engined. Apart from this, atmospheric pollution is practically nil. There is neither smoke nor fog and occasional dust storms provide the only foreign material in the atmosphere.

2. *Tobacco smoke.* Tobacco is certainly smoked by the Sudanese although it is not permissible to the orthodox Moslem. Five hundred and twenty-six tons of tobacco were imported from the United Kingdom in 1953, and the country itself produces a quantity. In addition tobacco is imported from Egypt. In spite of the price even the labourer in the towns smokes English cigarettes, and if the upper classes smoke, they consume as much as the average European smoker. Smoking is entirely confined to males. A number of the upper class Sudanese who have worked with and adopted European habits have smoked for the same period a comparable quantity of tobacco and, though this number cannot be large, this class has not so far suffered from lung cancer, and the evidence available, scanty and qualitative though it is, suggests that tobacco does not cause lung cancer in the Sudanese.

The most outstanding environmental difference between the indigenous Sudanese and European is that the former lives in an atmosphere practically uncontaminated by the exhaust of the internal combustion engine.

SUMMARY

1. One thousand, three hundred and thirty-seven specimens of malignant epithelial growths received in the Stack Laboratory, Khartoum, from 1935 to 1954 have been classified.

2. The site incidence of malignant epithelial tumours among the natives of the Sudan is found to vary materially in some respects from the European and from the African living in the United States of America. The greatest difference is in the relatively large numbers of cutaneous cancers seen among the native Sudanese. It is suggested that local environmental and not genetic causes account for this.

3. The breast and female genital tract are frequent sites for carcinoma in the Sudanese woman; it is probable they are as liable to contract this condition as their European counterpart.

4. Carcinoma of the stomach and colon are infrequent. It is probable that the rarity of gastric ulceration is related to the infrequency of gastric carcinoma. It is possible that the relative rarity of colonic carcinoma could be a racial trait. Malignant epithelial growths of most other organs are encountered among the Sudanese, but carcinoma of the lung is among the rarest.

ACKNOWLEDGMENTS

I have to thank Professor R. Kirk, O.B.E., M.D., F.R.C.P., F.R.S.Edin., for suggestion of this subject for investigation. Dr. Ahmed Ali Zashi, Director, Sudan Medical Service, for his permission to use the material, and Dr. Mansour El Haseeb, Director of the Stack Laboratories for Medical Research, Khartoum, for putting all the resources of the laboratories at my disposal.

REFERENCES

ABBOTT, P. (1956) *Trans. R. Soc. Trop. Med. Hyg.* **50,** 11.
ACKERMAN, L. V. (1948) *Amer. J. clin. Path.* **18,** 602.
AIRD, I. (1949) *Companion to Surgical Studies* **1,** 904 Edinburgh, Livingstone.
ANDERSON, W. A. D. (1941) *Surgery* **9,** 425.
ARCHIBALD, R. G. (1956) *Amer. J. Trop. Med. Hyg.* **50,** 11.
BERMAN, C. (1935) *S. Afr. J. med. Sci.* **1,** 12.
BISHOP, E. L. (1932) *Amer. J. Cancer* **16,** 522.
BONNE, C. (1937) *Amer. J. Cancer* **30,** 435.
COORAY, G. H. (1944) *Indian J. med. Res.* **32,** 71.
DAVIES, T. N. P. (1948) *East Afr. med. J.* **25,** 117.
DAWSON, J. W. (1925) *Edin. med. J.* **32,** 501.
DENOIX, P. (1947) *Bull. Inst. Nat. (d) Hyg.* **2,** 272.
DOLBEY, R. V. and MOORO, A. W. (1924) *Lancet* **1,** 587.
ELMS, B. G. T. and BALDWIN, R. T. B. (1947) *Ann. Trop. Med.* **41,** 321.
ENOS, W. F. and HOLMES, R. H. (1951) *Am. J. Path.* **27,** 523.
EVE, F. (1903) *Practitioner* **70,** 165.
GELFAND, M. (1949) *S. Afr. med. J.* **23,** 1010.
GEYER, A. (1947) *Bull. Soc. Path. exotique* **40,** 125.
GREISS, H. K. (1948) *J. Roy. Egypt. Ass.* **31,** 761.
HEWER, T. J. (1935) *J. Path. Bact.* **41,** 473.
HICKEY, B. B. (1957) *Brit. J. Surg.* **44,** 483.
HIGGINSON, J. (1951) *Cancer* **4,** 1224.
HOLLANDS, F. G. (1952) *Ann. Roy. Coll. Surg. Engl.* **5,** 265.
JANES, R. M. (1957) *Ann. Roy. Coll. Surg. Engl.* **21,** 1.
KIMBELL, C. W. A. (1954) *Proc. Roy. Soc. Med.* **47,** 895.
MAKAR, N. (1957) *Brit. J. Surg.* **45,** 240.
MEULING, R. J. and BURDETTE, W. J. (1950) *Zoologica* **35,** 12.
MORRIS, G. C. and HORN, R. C. (1951) *Surgery* **29,** 223.
NATH, V. and GREWAL, K. S. (1935) *Indian J. med. Res.* **23,** 149.
PRICE, A. S. (1940) *Urol. Cutan. Rev.* **44,** 56.
PRICE, P. B. (1928) *China med. J.* **42,** 505.
RANDALL, C. L. (1945) *J. Amer. med. Ass.* **127,** 20.
ROBINSON, H. B. G. (1937) *Arch. Path.* **23,** 831.
SHRECK, R. (1944 *a*) *Cancer Res.* **4,** 435.
———— (1944 *b*) *Cancer Res.* **4,** 119.
SMITH, E. C. and ELMS, B. G. T. (1934) *Ann. Trop. Med.* **28,** 461.
SNIJDERS, E. P. and STRAUB, M. (1924) *Trans. 5th Congr. Far East. Ass. Trop. Med.*
STEINER, P. E. (1954) *Cancer, Race and Geography.*
UYS, C. J. (1956) *Brit. J. Urol.* **28,** 75.
VINT, F. W. (1935) *Lancet* **2,** 628.
WILLIS, R. A. (1953) *Pathology of Tumours.* London, Butterworth.
WOODMAN, H. M. (1952) *East Afr. med. J.* **29,** 217.
WRIGHT, C. J. E. (1949) *J. Path. Bact.* **61,** 4.
WRIGHT, R. B., CLARK, D. H. and MILNE, J. H. (1953) *Brit. J. Surg.* **40,** 360.

ANATOMICAL MUSEUM

THE SPECIAL DISPLAY for the month of May consists of a series of specimens, probably incorporated into the College collection about 100 years ago, showing methods of protection by colour and form.

HYPERPLASIA AND METAPLASIA IN THE BRONCHIAL EPITHELIUM

An interim report on research work being carried out by

Professor G. J. Cunningham and Dr. D. P. Winstanley
Department of Pathology, Royal College of Surgeons of England

INTRODUCTION

THE BELIEF IS steadily gaining ground that most cases of carcinoma of the bronchus are due to the action of noxious substances in the inhaled air upon the bronchial epithelium. If this is true, then it is to be expected that malignant change would be preceded by epithelial hyperplasia similar to that seen in experimental carcinogenesis. Such changes might be looked for in the lungs of established cases of bronchial carcinoma, in the parts remote from the tumour, and also in the lungs of persons dying from other causes who had nevertheless been exposed to atmospheric pollution and cigarette smoke.

This report describes the results of a histological survey of material of these kinds. The first object was to define and classify the abnormalities in the bronchial epithelium, and next to determine their relative frequency, their distribution within the lung and their connexion with chronic bronchitis. Lastly, an attempt has been made to assess their relation to the smoking history.

REVIEW OF PREVIOUS WORK

Squamous metaplasia was the first abnormality to attract attention. It was described as a sequela of influenza (Askanazy, 1919 ; Wegelin, 1942) and in connexion with bronchiectasis and other chronic inflammatory conditions. Lindberg (1935) found transitional (stratified) epithelium in a series of cases of bronchial carcinoma and regarded certain epithelial downgrowths as potentially precancerous. Niskanen (1949) doubted whether squamous metaplasia was a precursor of cancer. Valentine (1957) believed that areas of squamous metaplasia might undergo transformation into carcinoma-in-situ.

Wittekind and Strüder (1953) divided epithelial metaplasia in chronic bronchitis into two types. The changes they describe do not conform to those met with in the present work and their classification has not been found to be applicable.

Weller (1953) distinguished two kinds of change—squamous and transitional metaplasia—and divided both into dormant and proliferative types. His criteria for proliferative activity are very similar to those used by other writers for carcinoma-in-situ, but he saw no metaplastic focus which he was able to diagnose as premalignant, carcinoma-in-situ, or minute carcinoma.

Auerbach *et al.* (1956, 1957), in the preliminary report of a large scale investigation, were the first to describe basal cell hyperplasia and intro-

duced a new classification of the abnormalities seen in bronchial epithelium. This classification is an advance on anything previously proposed and the present work has been based upon it. They found a remarkable parallelism between the incidence of hyperplastic changes and the cigarette consumption and they diagnosed carcinoma-in-situ in a surprisingly large proportion of their cases. Hamilton *et al.* (1957), in a small series of post-mortem cases, reached conclusions similar to those of Auerbach *et al.*

Chang (1957) introduced a method of examining whole mounts of the bronchial epithelium and also cut conventional sections. He drew attention to the frequency of abnormal nuclei in hyperplastic areas, a finding also noted by Bassermann (1957) in smears of bronchial mucus.

MATERIALS AND METHODS

Most of the post-mortem specimens have been obtained at necropsies carried out for H.M. Coroner ; a few were derived from hospitals. No selection has been exercised ; it has, in fact, been difficult to secure an adequate amount of well preserved material because of the rapid post-mortem desquamation of the bronchial epithelium. Fixation within twelve hours of death is essential; when necropsy has to be deferred beyond this time the bronchial tree is filled with formalin injected through the cricothyroid membrane. The lobes of the lung are separated from one another and sliced at right angles to the segmental bronchi. Auerbach *et al.* (1956) cut the entire bronchial tree into blocks—over 200 in all—but we believe that a smaller number (nineteen) provides a representative sample. Of the forty-four post-mortem specimens so far examined, thirty-one were sufficiently well preserved to merit inclusion.

The surgical material consists of lungs or single lobes resected for cancer of the bronchus. Prompt fixation ensures good preservation of the epithelium. Up to the present, sixty-nine specimens have been examined ; smoking histories are available for forty-seven of them.

RESULTS

Before describing the abnormalities met with in the bronchial epithelium it is necessary to mention the cases in which no abnormality was discovered (Fig. 1). Nine of the thirty-one post-mortem specimens came under this heading. One of these was a child of two years ; four were old women who were non-smokers or whose smoking habits were unknown ; and four were old men who had all been smokers. One of the men had smoked twenty cigarettes a day up to his death at eighty from spheroidal cell carcinoma of the bronchus. Two of the others smoked five and sixteen cigarettes a day, while the last, who had given up smoking forty years ago, had an undifferentiated bronchial carcinoma.

Of the forty-seven surgical patients whose smoking histories are known, seven men had normal bronchial epithelium. Their ages ranged from forty-nine to sixty-six years. Three of them had smoked over twenty cigarettes a day for many years.

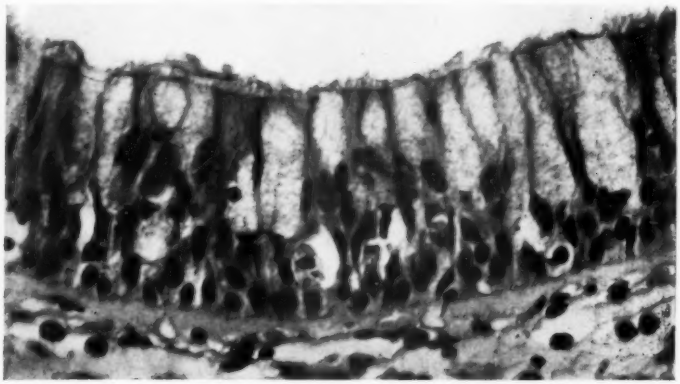

Fig. 1. A woman of sixty-seven whose smoking habits are not known. Section from the left main bronchus. H. and E. ×500. Normal bronchial epithelium with one to two layers of basal cells.

The abnormalities in the bronchial epithelium are classified as follows :

1. Basal cell hyperplasia.
2. Squamous metaplasia.
3. Stratification or transitional change.
4. Epithelial irregularities and carcinoma-in-situ.

1. Basal cell hyperplasia

Multiplication of the layers of the basal cell zone is a common finding (Fig. 2). Although the cells do not lie in regular layers and an exact count is not possible, a useful approximation can be arrived at. We follow Auerbach's (1956) grading :

3-4 layers	—	mild	basal cell hyperplasia
4-6 layers	—	moderate	
7 or more layers	—	advanced	

In the deeper layers the oval nuclei retain their normal perpendicular orientation. Near the surface they become paler and more rounded. These variations are comparatively slight and there is no change in the nuclear-cytoplasmic ratio. Mitoses are very scanty but giant nuclei, usually about twice the size of normal nuclei, are sometimes seen. Giant cells are occasionally found with up to four nuclei of normal size, packed together inside the cell without much increase in cytoplasm. They may occur in comparatively normal epithelium and are not always associated with other nuclear irregularities or with disorganized epithelium.

Basal cell hyperplasia occurs in all parts of the bronchial tree, though it is more frequent and usually more advanced in the larger bronchi. It may be confined to small patches or it may spread uniformly round an entire bronchus.

Fig. 2. A man of sixty who smoked twenty to thirty cigarettes a day. Section from the trachea. Periodic acid-Schiff. ×500. Advanced basal cell hyperplasia (up to eight layers of cells) with surviving goblet cells near the surface.

Of the thirty-one post-mortem cases, nine had a mild degree of basal cell hyperplasia. Unfortunately, a smoking history is available for only one of these, a woman of seventy-five who smoked one or two cigarettes a day. Among the four cases with moderate basal cell hyperplasia were a man of seventy-eight who smoked ten cigarettes a day, and a woman of seventy-seven, a non-smoker. The three cases with advanced basal cell hyperplasia were elderly men who smoked sixteen, twenty and twenty to thirty cigarettes a day respectively. Basal cell hyperplasia of some degree was found in twenty-one of the forty-seven surgical cases. In five of them it was mild, in nine moderate, and in seven severe. No correlation with smoking habits was apparent.

2. Squamous metaplasia

This change is quite different from basal cell hyperplasia. The entire thickness of the epithelium is involved and as a rule it resembles the normal stratified squamous epithelium of the mouth or oesophagus. The cells are comparatively large and flattened. The nucleus is large, pale and vesicular. Intercellular bridges are conspicuous and constitute a diagnostic criterion, but keratinization has not been observed. The metaplastic epithelium is often many layers thick and sometimes has papillae which project into the lamina propria. It is more resistant to post-mortem desquamation than normal epithelium.

In distribution squamous metaplasia shows the same centripetal tendency as basal cell hyperplasia but it often occurs in sharply localized

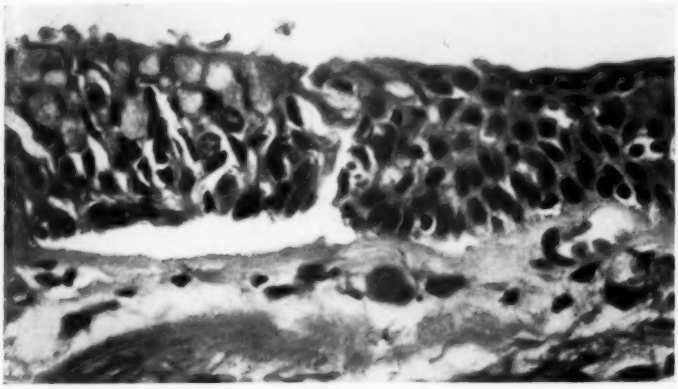

Fig. 3. A man of sixty-six—a smoker. Section from the left upper lobe bronchus. H. and E. ×500. A localised patch of squamous metaplasia, sharply demarcated from normal epithelium.

patches (Fig. 3). It is sometimes confined to the spurs of bifurcations and the crests of longitudinal ridges. The boundary between metaplastic epithelium and the adjacent normal epithelium is often quite abrupt. The lamina propria beneath patches of metaplastic epithelium often shows evidence of chronic inflammation : fibrosis, infiltration with lymphocytes, and increased vascularity.

Squamous metaplasia was present in ten of the thirty-one post-mortem cases. No correlation with age, severity of bronchitic changes, or smoking history is yet apparent from these small numbers, but it is noteworthy that in the three cases with severe basal cell hyperplasia squamous metaplasia was found in addition.

It was present in twenty-five of the forty-seven surgical cases ; in some of these it was very mild. Three of them were pipe smokers ; the cigarette consumption of the others ranged from six to fifty a day. Most of them showed mild bronchitic changes, but there was no obvious association between squamous metaplasia and chronic bronchitis.

3. Transitional change

Certain intermediate types, difficult to classify, are found in a few cases. In these the epithelium is several layers thick, the superficial layers being stratified while the deep layers retain the usual characters of basal cells. The columnar cell layer is absent : this point can be verified by staining with periodic acid-Schiff to reveal any remaining goblet cells. Sometimes the appearance of urinary epithelium is closely simulated. Intercellular bridges and other features of squamous epithelium are lacking.

The nature of this change is obscure. In some cases it probably represents basal cell hyperplasia in which the columnar cells have been lost. In others it may be a precursor of squamous metaplasia.

Transitional change of this type has been observed in six of the post-mortem cases, usually only in small areas. No correlation with the factors previously considered is apparent. It has been observed in ten of the surgical cases, in continuity with areas of squamous metaplasia.

4. Epithelial irregularities and carcinoma-in-situ

Disorganized epithelium has so far been observed in a few cases, in none of which it fulfils all the criteria of carcinoma-in-situ (Fig. 4). In our examples the nuclei are hyperchromatic and vary in size and shape, but there is still some cellular differentiation and only a few mitoses are apparent. Sometimes multiple nucleoli are present; the significance of this change is not clear.

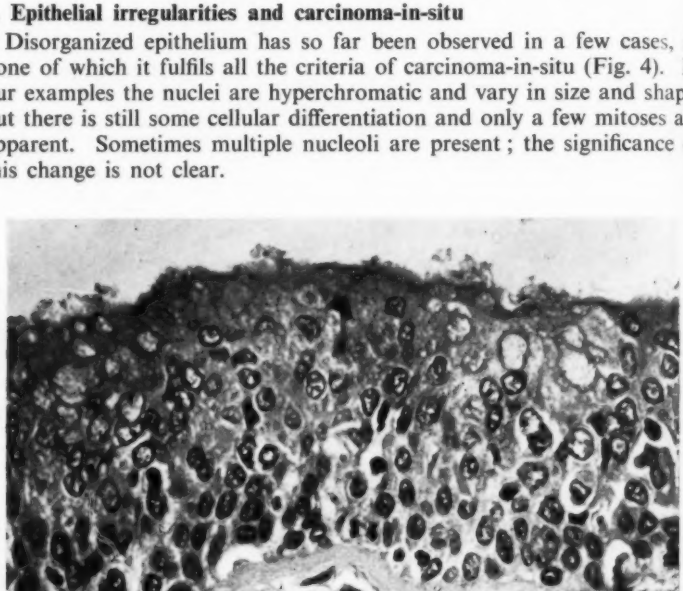

Fig. 4. A man of fifty-five who smoked fifteen cigarettes a day. Section from the carina. H. and E. ×500. A patch of irregular epithelium with a mitosis.

In the thirty-one post-mortem cases epithelial irregularities of this kind have been observed in three; among the forty-seven surgical cases, in four only.

DISCUSSION

The number of cases so far available is too small to permit definite conclusions to be drawn, but it is already evident that changes of all the kinds described by previous workers are to be found in our material and some provisional interpretations are possible.

The bronchial epithelium may be perfectly normal in heavy smokers, even in men who have smoked from adolescence and reached a consumption of forty cigarettes a day. It is also clear that the epithelium in the neighbourhood of a bronchial carcinoma may be normal. Nevertheless, epithelial abnormalities are common in both these conditions and it seems possible that a more detailed search might reveal abnormalities which are overlooked if only a few blocks are taken.

Basal cell hyperplasia is a common and conspicuous change. There is often a similarity between the hyperplastic basal cells and the cells of oat cell carcinomas. Whether this is more than a superficial resemblance remains to be proved. We have found nothing to contradict Auerbach's (1956) suggestion that basal cell hyperplasia is connected with cigarette smoking.

The frequency of squamous metaplasia has long been recognized and our observations have so far provided nothing new. We agree with Weller (1953) that patches of squamous metaplasia vary in activity, some being dormant while others show vigorous proliferative changes. It is possible that the latter may be precancerous.

Basal cell hyperplasia and squamous metaplasia tend to be centripetal. In many specimens these changes are most advanced at the carina, rather less severe in the main bronchi and progressively less intense in the lobar and segmental bronchi. This pattern is in accordance with the work of Macklin (1956) who showed that although the entire tracheobronchial tree is vulnerable to noxious substances in the air, the parts exposed to the most concentrated and sustained attack are the large bronchi near the carina.

We have seldom observed changes which could be regarded as intermediate between basal cell hyperplasia and squamous metaplasia, and we have never met with appearances which we interpreted as indicating a transition from one type to the other. As a working hypothesis, we regard the two types of change as differing in kind and not merely in degree. In the hope of throwing further light on the differences between them, we are paying special attention to nuclear structure and applying histochemical methods to some of our material.

The nature of transitional change is still obscure, but the absence in epithelial activity makes it unlikely that it plays any important part in the genesis of cancer.

We cannot confirm Auerbach's (1956, 1957) findings on the frequency of carcinoma-in-situ. We have found areas showing intense proliferative changes but in none of them have we been satisfied that all the criteria of carcinoma-in-situ have been fulfilled. Nevertheless, in border-line cases the diagnosis is open to differences of opinion and our disagreement is probably one of interpretation rather than observation.

In conclusion, it has become apparent that the responses of bronchial epithelium to noxious stimuli are comparatively restricted and we have

reached a stage in the work at which we expect to observe no new histological abnormalities. Our remaining task is to collect enough material to enable us to analyse the changes in greater detail and to extend our observations by certain histochemical techniques ; these are already under trial.

ACKNOWLEDGMENTS

We wish to express our thanks to Sir William Bentley Purchase, Dr. F. E. Camps, Dr. G. T. Allen, Dr. Horace Joules, and Dr. R. A. B. Drury for their help in obtaining material. We are also grateful to Drs. K. R. Stokes and E. Nassau, of Harefield Hospital, for permission to make use of surgical specimens.

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REFERENCES

ASKANAZY, M. (1919) *Korresp-Bl. schweiz. Ärz.* **49**, 465.
AUERBACH, O., GERE, G. B., FORMAN, J. B., PETRICK, T. G., SMOLIN, H. J., MUEHSAM, G. E., KASSOUNY, D. Y., and STOUT, A. P. (1957) *New Engl. J. Med.* **256**, 97.
———— PETRICK, T. G., STOUT, A. P., STATSINGER, A. L., MUEHSAM, G. E., FORMAN, J. B., and GERE, J. B. (1956) *Cancer (Philad.)*, **9**, 76.
BASSERMANN, F. J. (1957) *Thoraxchir.* **4**, 464.
CHANG, S. C. (1957) *Cancer (Philad.)*, **10**, 1246.
HAMILTON, J. B., SEPP, A., BROWN, T. C., and MCDONALD, F. W. (1957) *Canad. med. Ass. J.* **77**, 177.
LINDBERG, K. (1935) *Arb. path. Inst. Univ. Helsingf.* **9**, 1.
MACKLIN, C. C. (1956) *J. thorac. Surg.* **31**, 238.
NISKANEN, K. O. (1949) *Acta. path. microbiol. scand.*, Suppl. 80.
VALENTINE, E. H. (1957) *Cancer (Philad.)*, **10**, 272.
WEGELIN, C. (1942) *Schweiz. med. Wschr.* **72**, 1053.
WELLER, R. W. (1953) *Amer. J. clin. Path.* **23**, 768.
WITTEKIND, D. and STRÜDER, R. (1953) *Frankfurt. Z. Path.* **64**, 294, 405.

APPOINTMENT OF FELLOWS AND MEMBERS TO CONSULTANT POSTS

D. G. JAMES, M.D., M.R.C.P., M.R.C.S.	Consultant Physician to Royal Northern Hospital.
J. N. ASTON, M.B., F.R.C.S.	Consultant Orthopaedic Surgeon to Mount Vernon Hospital.
W. BRUMFITT, M.B., M.R.C.P., M.R.C.S.	Consultant Clinical Pathologist to Edgware General Hospital.
I. YENTIS, M.D., M.R.C.P., F.F.R.	Consultant Radiologist to Windsor Group of Hospitals.
K. TILL, M.B., F.R.C.S.	Consultant Surgeon to the Hospital for Sick Children, Great Ormond Street.

The Editor is always glad to receive details of new appointments obtained by Fellows and Members, either through the Hospital Boards or direct.

RECENT OVERSEAS VISITORS TO THE COLLEGE

RECENT OVERSEAS VISITORS to the College have included Mr. and Mrs. M. P. Susman from Sydney, who attended the monthly dinner in April.

A CURATOR'S CURIOSITY

by

Jessie Dobson, B.A., M.Sc.

Curator of the Anatomy Museum, Royal College of Surgeons of England

IN THE Annual Report on the Museum prepared by the Conservator in 1924 the following acquisitions are noted :

Artificially deformed skull of a woman aged 18 from a Coptic cemetery of fifth century A.D. at El Fachin, Upper Egypt. The deformity is similar to that met with in Georgian graves of the Bronze Age.

A miniature wax restoration of the woman with the deformed skull mentioned above. The deformity was common among women of Akenaton reign's.

The donor was Professor Douglas Derry of the School of Anatomy in Cairo.

Now the wording of these two descriptions rather suggests that some difficulty had presented itself with regard to the dating of the skull and further investigation has proved that this was indeed so.

In 1918, Gorgy P. G. Sobhy, then a member of the staff of the Anatomical Department of the School of Medicine in Cairo, published in the *Bulletin de l'Institut Français d'Archaeologie Orientale du Caire* (T. XIV. 65-67) a paper entitled ' Description d'un Crâne trouvé dans une tombe à Tell-el-Amarna " in which he puts forward a most plausible and exciting suggestion which, however, unfortunately lacks factual support. The skull was the property of Dr. L. Gatineau, Surgeon-Dentist to the French Hospital in Cairo, who had permitted him to examine it and publish his findings. Dr. Sobhy points out that many representations of Akenaton (Amenhotep IV) and of his daughters show the same curious elongation of the head seen in this skull and he mentions in particular a fresco found at Tell-el-Amarna, now at the Ashmolean Museum in Oxford, showing two of the princesses with this characteristic which, furthermore, was only found in members of this royal family. He confidently asserts that the skull belonged undoubtedly to a female relative of Amenhotep IV, living, that is, in the fourteenth century B.C. The illustrations to this paper consist of front and side views of (*a*) the skull with some of the integument still adherent ; (*b*) the skull in its cleaned condition ; (*c*) a wax model prepared by Dr. Gatineau and signed by him, showing the presumed appearance during life.

Four years later, in the journal *La Semaine Dentaire* (Paris, 22nd January, 1922), Gatineau himself published an article with the title " Crânes de martyrs Coptes Chrétiens provenant de Medall, près Fachn (Haute-Egypte) ' relating to excavations carried out by him on this site in collaboration with His Excellence Daninos Pacha. The mummified bodies that were found here were thought to be the victims of a massacre who had been buried by the survivors, the evidence for this being that they were found " placés les uns à côté des autres, avec assez d'ordre." Judging by the wrappings, it was estimated that this presumed massacre

had taken place during the time of Justinian I when a considerable amount of persecution of the Coptic Christians was known to have taken place. Figure 2 in this paper is the same as Figure (*a*) in Sobhy's account.

A year later, in 1923, Dr. Sobhy, published a note in the *Journal of Egyptian Archaeology* (Vol. IX, p. 117) saying that he had been wrongly informed " by the finder of the skull " that it had come from Tell-el-Amarna. In the same year, the skull and the wax model came into the possession of Professor Derry who brought them to London and sold them to the College for the sum of £6. After his return to Cairo,

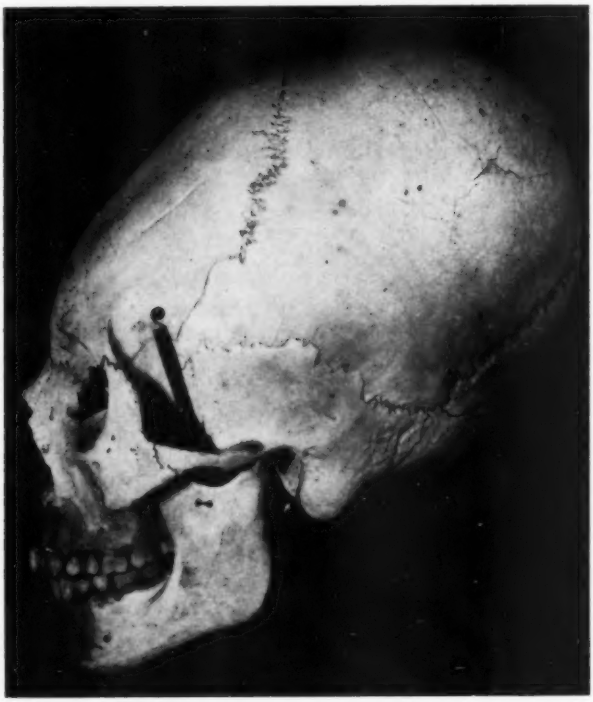


Fig. 1. The artificially deformed skull.

application was made to him from the College as to which of the two accounts should be taken as authentic. The following are extracts from his reply : " . . . you may I think rely on the statement that the remains unearthed by Gatineau were those of Copts . . . but I should leave the date severely alone. All the massacre business should also be left out, it is probably nonsense, but only an examination of the actual skulls would

tell us whether the fractures were produced post or ante mortem. Burials in rows close to one another but in separate graves are quite common and no evidence of massacre any more than it is at Kensal Green, and Ptolemaic-Roman mummies would be expected, as the cemetery had probably been used for centuries. The presence of the artificially deformed skull hitherto unknown in Egypt, is additional evidence in favour of Christians, that is if it really came from Georgia, and we do not know I think of any other place in this region of the world where this is practised. My Curator, Dr. Boulgakow, tells me it is still done in one village in that country. So when everything is boiled down we are only justified in saying that the skull came from excavations at Medall, Upper Egypt, of Coptic date, that is anything from first to sixth century A.D.; that it

Fig. 2. Front view of the wax model.

exhibits a form of distortion obviously artificial, and quite unknown in Egypt; but that its presence in a Christian cemetery *might* indicate that it belonged to a person from the only Christian country of which we have any knowledge as practising this method of deformation."

But this is not the end of the story. On 5th November, 1927, an article written by Warren R. Dawson appeared in the *Lancet* (2. 1001) on the subject of Artificial Deformation of the Skull. Here the author mentions that Professor Elliot Smith had come to the conclusion that the skull of Akhenaten whose tomb had been found in 1907, showed signs of

hydrocephalus, a view that was supported by Professor A. R. Ferguson; and he remarks also that the daughters of Akhenaten and Nefertiti were "always represented on contemporary monuments with heads of a very peculiar shape, and, as in the case of Akhenaten himself, this had hitherto been held to be no more than a convention arising out of the novel artistic concepts which came into vogue at the time. In 1924 Professor Elliot Smith expressed the view that the childrens' heads might have been subjected to the process of artificial deformation (Elliot Smith and Dawson: *Egyptian Mummies*. London. p. 96). At the time this suggestion was advanced he was not aware that the material for solving the mystery was already in existence" . . . and Dawson goes on to give a brief resumé of Dr. Sobhy's paper of 1918, making the comment: "There is no evidence to prove whether or not this skull belonged to a member of Akhenaten's family, but it does at least prove that artificial deformation was being practised in Egypt during his time and suggests that the form

Fig. 3. Side view of the model showing Dr. Gatineau's signature.

of Akhenaten's head, pathologically deformed by nature, may have been deliberately copied by artificial means in the case of his daughters."

Three weeks later, on 26th November, a letter from Mr. Dawson appeared in the *Lancet* (ibid. p. 1166) in which he states that Gatineau's paper of 1922 and Sobhy's note of 1923 had been brought to his notice. "I am endeavouring," he says, "to ascertain the truth of the matter, but in the meantime I wish to withdraw any conclusions that may depend upon the authenticity of this skull. My original suggestion, however, that the heads of Akhenaten's children may have been deliberately deformed in

imitation of their father's is not affected by eliminating from the discussion the skull mentioned above."

A month later, on 24th December, a letter from Professor Derry was published in the *Lancet* (ibid. p. 1376) and as this clears up many points it will be reproduced here in full :

" My attention has been called to an article by Mr. Warren R. Dawson, in which the writer draws conclusions as to the origin of the practice of artificial deformation of the skull in Egypt from what he honestly believes to be evidence for such a custom, but which, unfortunately, as will be seen, is only evidence of the way in which facts may be distorted to suit the purposes of persons more interested in making a story than in truth.

Fig. 4. The skull of Amenhotep IV (Akhenaten).

The skull upon which Mr. Dawson bases his suggestion was found by Dr. L. Gatineau in a Coptic cemetery of about the fifth century A.D. at Medall, near Fachn, about 100 miles from Cairo. It was brought to Cairo, and subsequently was stated to have come from Tell-el-Amarna, nearly 100 miles further south, from the ruins of the town of Akhenaten. Dr. Gorgy Sobhy, on the strength of this statement, and from the *seeming* resemblance of the skull in shape to the heads of Akhenaten, his daughters and other people represented on the monuments and in the statues of the period, examined and measured the skull but made no restoration of it. He, however, gave it as his belief that it belonged to a female member of the family of Akhenaten, and published his account in the *Bulletin de l'Institut Français*, t. XIV, with photographs both of the skull

and of a wax model made by Dr. Gatineau, to represent what he imagined would be the appearance of a woman with a skull of this shape. If, however, the skull and the model are examined, it will be seen that while the model resembles the stone heads from Tell-el-Amarna, it in no way agrees with the skull upon whose shape it is supposed to be based. The peculiarities of the deformed skull, due to the method of bandaging which has been employed to distort it, are its length, narrowness, and height, whereas the statues are remarkable for their width and flatness, as are also the actual skulls of both Akhenaten and Tut-ankh-Amen.

The skull is undoutedly an example of artificial deformation by bandaging and the fact that it was taken from a Christian cemetery lends colour to my suggestion that the girl was a visitor to Egypt from the Caucasus, where the practice is, I am told, still in vogue.

In 1923, hearing that Dr. Gatineau was selling his effects, I bought the skull and wax model and took them to London. They were purchased for the Museum of the Royal College of Surgeons, where they may be seen.

In the meantime, Dr. Gatineau had himself published a short note of his excavation at Medall, and in this he gives photographs of some of the skulls found there which he calls "Crânes de martyrs Coptes chrétiens" and includes in Figure 2 of his paper the photograph of the skull already described and published in 1918 as coming from Tell-el-Amarna ! As I write I have in front of me the two papers, in each of which the same photograph appears, the one in Dr. Gatineau's paper, labelled fifth century A.D., and its provenance given as Medall, the other paper, that of Dr. Sobhy, describing the skull as that of a member of the family of Akhenaten, whose town lies 100 miles south of Medall and whose date is some eighteen hundred years earlier ! On making this discovery I communicated with Dr. Sobhy who thereupon published a correction in the *Journal of Egyptian Archaeology*, Vol. ix. p. 117. This correction Mr. Dawson has unfortunately not seen. [Nor had Professor Derry seen Mr. Dawson's second letter, apparently.]

In the whole of my experience in Egypt where I have seen and handled many thousands of crania of all dates, I have never come across another example of deformation by bandaging, and it may be taken as certain that the custom did not have its origin in Egypt nor was practised in this country."

In 1931, Eric John Dingwall published his comprehensive work on Artificial Cranial Deformation and includes among the illustrations one of this specimen which he calls the "Medall Skull" (Plate VI*b*). In his comments, the author notes that, on the evidence afforded by representations of individuals on monuments and otherwise of the Akhenaten period elongated heads were not confined to the royal family. "Let us assume," he says, "for the sake of argument that actual artificial cranial deformation was practised in Egypt during the Akhenaten period in order possibly to imitate the shape of the King's skull which, through pathological causes was of abnormal form. A number of difficulties, however, immediately present themselves. No skulls showing forms in the least resembling those shown in the portraits of the princesses have been found in Ancient Egypt. This does not prove that cranial deformation was never practised in that country but it does suggest the possibility of it. We have not a great number of skulls from Tell-el-Amarna, and the remains of the princesses have unfortunately not yet been discovered. Now this theory involves the assumption that the Egyptians having noted the form of their King's skull, proceeded according to the dictates

of a new fashion to deform artificially the heads of his daughters, and, without any previous practice, succeeded in devising just that form of constriction which would produce the desired result. This is certainly not impossible but some may think it improbable. . . . What is worthy of note is that at the time of Akhenaten we have what at present is the earliest date at which persons are represented with skulls of a consistently abnormal shape."

Examples of head moulding from other parts of Africa are common; and it may well be that, as Professor Derry suggests, this skull now in the College belonged to a visitor to Egypt, possibly from Georgia.

The main problem, therefore, remains as tantalising and insoluble as ever—what is the date of this skull? If the *finder* gave the information to Dr. Sobhy that it came from Tell-el-Amarna, who was he if it was not Dr. Gatineau who, presumably, would not have made such a mistake? Although the evidence to be gained from the skull itself points to it being that of a female not older than the early twenties, one would hesitate to be so positive about the age as given in the 1924 Report; and was the wax model, in fact, made as a reconstruction from this particular skull, or was it prepared to give a general idea of the possible appearance in life of the female members of the royal family during the fourteenth century B.C.? Since the skull and the model were brought back to the College with the rest of the collection after the end of the war, they have remained unlabelled and from that very fact seem to attract the notice of the visitor; but whereas the above story is interesting enough to relate to the chance enquirer, the problem still remains of allotting these specimens to their appropriate places in view of the regrettably few *facts* that are available.

CEREMONY OF PRESENTATION OF DIPLOMAS

THE SECOND ANNUAL ceremony for the presentation of diplomas will take place on Wednesday, 10th June, beginning at 2.30 p.m.

The occasion will be a General Meeting of the College open to Fellows, Members and other diplomates of the College, and in the presence of this General Meeting there will be a meeting of the Council at which an Honorary Fellow, Elected Fellows and an Elected Fellow in the Faculty of Anaesthetists will be admitted and diplomas will be granted to the candidates successful at the Final Fellowship Examination in May. The Honorary Fellow to be admitted on this occasion will be Dr. Paul Hawley, the Direcor of the American College of Surgeons, and he will also deliver an Adress to the newly admitted diplomates.

Fellows, Members, Fellows and Licentiates in Dental Surgery, and Fellows in the Faculty of Anaesthetists, whose diplomas have been granted after examination during the past year and who have indicated a wish to attend the ceremony, will be presented according to their medical or

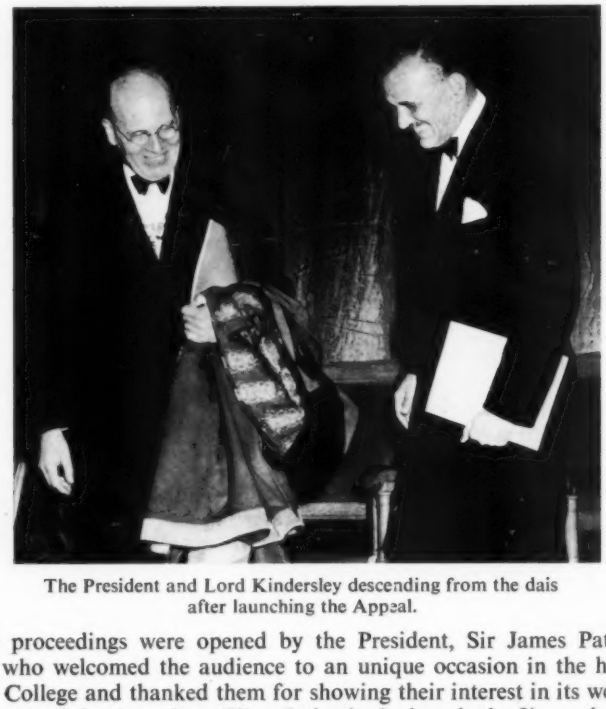
dental school by a member of Council or Court of Examiners or appropriate Board of Faculty, and will individually receive their diploma from the President.

Fellows and other diplomates are most welcome to attend, and it is hoped that those who possess the academical dress of the College will wear it.

LIFE IN EMERGENCY WARD 10

TO MARK THE opening of the College's Appeal for funds there was shown in the Edward Lumley Hall the première of the film " Life in Emergency Ward 10 " in the evening of 24th March.

The hall was packed to capacity and the audience included not only Fellows of the College but also many of its generous donors and representatives of those to whom the appeal is addressed, representatives of Eros Films, and several members of the cast.



The President and Lord Kindersley descending from the dais after launching the Appeal.

The proceedings were opened by the President, Sir James Paterson Ross, who welcomed the audience to an unique occasion in the history of the College and thanked them for showing their interest in its welfare. He expressed thanks to Eros Films Ltd. who had made the film and whose chairman, Mr. Philip Hyams was present, and to the R.A.M.C. Band

who had played by permission of Sir Alexander Drummond. He described the occasion as the culmination of efforts to tell the public about the work of the College, efforts which had been going on for a year with the help of the Press and B.B.C. He invited the guests not only to see the film but also to inspect those of the scientific departments which would be on view afterwards. The President described the film as first class entertainment and a magnificent picture of hospital life, on which

The President greeting Miss Christina Gregg who played the part of one of the nurses in the film.

he congratulated Eros Films and all the players. In real life the surgeons might not all be as handsome as the actors, but they would all be Fellows of this College, and it was this College, which by its educational activities, was responsible for the present high standards of surgery. The film depicted the scientific work lying behind surgery to-day, instanced by the exciting heart-lung machine, but it also gave the lie to the fallacy that science was driving humanity out of surgery, and brought out extremely well the tremendous amount of care for the individual patient and his relatives.

The film was then shown. It was referred to, with illustrations, in the April *Annals*.

Afterwards, the President again mentioned the heart-lung machine which had been largely designed in the College, and spoke of the work

of the College Departments in research and post-graduate education, which was bound to cost a very great deal. The collection of the money was a very big task, but the Appeal Committee was very influential with Lord Kindersley as chairman and Sir Simon Marks as vice-chairman. He expressed the enormous debt of the College to Lord Kindersley for organising the appeal, and giving to it so much time and thought and energy. Sir Simon Marks, a dear friend and an Honorary Fellow, had given the College not only a great deal of financial help, coming from himself and his family, but also tremendous encouragement derived from his great enthusiasm.

Lord Kindersley then spoke and began with his father's well remembered " Good evening, everybody." He added his praise and congratulations to Eros Films for their brilliant production. Speaking of the College, he said it had with exaggerated modesty kept its light under a bushel and was at last emerging from purdah, willing to give the world an insight into its tradition and tell the world what goes on behind its façade to Lincoln's Inn Fields. As an experienced surgical patient, he doubted whether one in thousands realised what they owed to either the surgeon himself or the Royal College of Surgeons. He was in the secret and knew of the continuous battle going on in the College, a battle of research, and teaching and learning with the aim of improving the arts and skills to save lives, prevent and cure disease and bring relief to pain and suffering. More than 1,000 young doctors were passing through the lecture rooms of the College each year, and they were drawn from all parts of the Commonwealth and would go out to spread the powerful influence of the College throughout the English speaking world. In the promotion of surgery the College must keep pace with the changes of contemporary life, and must advance in order to maintain leadership of the world in the art and science of surgery. They must have equipment, lecture rooms, and all that they needed : the slogan was " give us the tools and we will do the job."

Lord Kindersley declared it unthinkable that this country could fail to meet the challenge : it was for £350,000 to complete the building and an additional income of £150,000 per annum to maintain the work of the College : that meant a capital sum of £3,000,000. He was enormously encouraged by the gifts already received, and he recited an impressive list of donations from individuals, firms, charitable trusts, and Fellows of the College. It was a great lead, and he begged all of those present who had influence on company boards to use their most persuasive manner in obtaining a really substantial donation. He concluded " I would just add that I have never chaired an Appeal before, and I think if I were to start life again (and I have said this for many years) I would try to become a Surgeon, and I suppose for that reason I have been drawn to chair this Appeal which I do with very great pleasure and I hope we will be able to say with success."

In Memoriam

SIR WALKER SHEPHERD, 1895-1959

THE DEATH OF Sir Walker Shepherd in Canada on 28th February is a severe blow to the College, to which he had shown himself to be a firm friend. His advice and support as a member of the Appeal Committee was invaluable. It was very largely due to his interest and practical advice that the Faculty of Dental Surgery was able to raise sufficient funds to maintain the new Department of Dental Science for its first crucial years of existence. His election by the Council as an Honorary Fellow in Dental Surgery was a tribute not only to the invaluable services he had rendered to the Faculty, but to those personal qualities of friendship and understanding that had made him so welcome in the College.

He might justly be said to have typified all that is best in that new race of benefactors on whom the medical profession depends so much today; those, that is, who do not possess large private fortunes which they can bestow on charitable and scientific objects, but who, by their leadership and enthusiasm, encourage great industrial and commercial concerns to support worthwhile projects in research and education. Like Lord Nuffield, Sir Walker Shepherd had the vision and understanding to bring help effectively where it was most needed and would bring the best results.

Originally a student of theology, he became a soldier in the First World War, and, when he turned later to industry, concern for human suffering and a determination to dispel ignorance, born of his war experience, remained with him. He was held in the highest esteem by his colleagues in industry and by all those abroad who saw in him an outstanding example of the high ideals and practical ability for which this country is honoured and respected throughout the world.

It is comforting to recall what pleasure his association with the College gave to him, and to Lady Shepherd, to whom in her loss the College extends its sincerest sympathy.

PROCEEDINGS OF THE COUNCIL IN APRIL

AT A MEETING of the Council, on the 9th April 1959, with Professor Sir James Paterson Ross, President, in the Chair, Professor J. McMichael, F.R.S., of the Postgraduate Medical School of London, was appointed a Sir Arthur Sims Commonwealth Travelling Professor to visit Australasia in 1960. Mr. Douglas Robb, C.M.G., Surgeon, Greenlane Hospital, Auckland, was appointed a Sir Arthur Sims Commonwealth Travelling Professor to tour Britain and parts of Africa in 1960.

Professor C. G. Rob of St. Mary's Hospital was admitted to Membership of the Court of Examiners.

Mr. J. A. Shepherd (Liverpool) was admitted as a Fellow elected *ad eundem*.

The following were elected Fellows of the College without examination as being Medical Practitioners of twenty years' standing: Dr. A. H. Bennett (Northwich); Dr. S. F. Logan Dahne (Reading); Sir Joseph Pierre (Trinidad); Dr. C. MacPherson, C.M.G. (Newfoundland); Mr. A. T. Britten Jones (Adelaide); Professor A. J. E. Cave (St. Bartholomew's Hospital).

Mr. L. E. C. Norbury was appointed Gordon-Watson Lecturer.

A Moynihan Lectureship was awarded to Dr. Bradley Coley of New York and a special Lectureship to Dr. Barry Anson of Chicago.

Dr. E. F. Scowen was appointed an Imperial Cancer Research Fund Lecturer for 1960.

The Council selected the following subject for the Jacksonian Prize for 1960: "The Aetiology, investigation and treatment of renal calculus."

One diploma of Membership was granted.

Dr. Ashley Daly and Dr. H. R. Griffith were elected Honorary Fellows in the Faculty of Anaesthetists, and the following were elected Fellows in that Faculty without examination: Dr. R. H. P. Fitzpatrick (Sidcup); Dr. A. Goldblat (Brussels); Dr. T. Gordh (Stockholm, Sweden); Dr. G. A. Haydock (York); Dr. E. Nilsson (Lund, Sweden).

One Diploma of Fellowship in the Faculty of Anaesthetists was granted (by examination) and six diplomas in Orthodontics were granted.

Diplomas were granted, jointly with the Royal College of Physicians, as follows: Ophthalmology (27), Radio-Diagnosis (27), Radiotherapy (10), Child Health (117), Physical Medicine (6), Tropical Medicine and Hygiene (42), Psychological Medicine (1), Public Health (1).

The following hospitals were recognised under paragraph 23 of the Fellowship Regulations:

Hospitals	Posts Recognised		
	General (6 months unless otherwise stated)	Casualty (all 6 months)	Unspecified (all 6 months)
Stoke-on-Trent—City General Hospital (Additional)			*Under para. 23* (c) S.H.O. (E.N.T.)
Harrow—Harrow Hospital	Regr.	Cas. Off.	
Brighton & Lewes Group—Sussex Throat and Ear Hospital, Royal Sussex County Hospital and Royal Alexandra Hospital (additional)			*Under para.* 23 (c) Regr. (E.N.T.) S.H.O. (E.N.T.)
Dover—Royal Victoria Hospital (additional)	S.H.O.		
Coventry—Coventry and Warwickshire Hospital (redesignation)			*Redesignation of* J.H.M.O. (Orth & Traumatic) as Regr.
Middlesbrough—North Ormsby Hospital (redesignation)	*Redesignation of* 2 H.S.s as H.S. or S.H.O. posts		
London—Tilbury & Riverside Hospital (Mr. Edwards)	*Temporary recognition for further* 2 *years until June*, 1961 2 Surg. Regrs.	Cas. Off.	

DONATIONS

DURING THE LAST month the following generous donations have been received :

Appeal Fund:

£5,000 M. Samuel & Co. Ltd.
£1,000 Andrew Weir & Co. Ltd.
£250 Lazard Brothers & Co. Ltd.
£250 Watneys Ltd. (Stag Charitable Trust.)
$500 Victor Saville.
£150 Low & Bonar, Ltd.
£105 A. R. B. Owen.
£105 Charrington & Co.
£105 W. & A. Gilbey, Ltd.
£105 W. Greenwell & Co.
£105 Brown, Shipley & Co.
£105 G. H. Thomas (further gift).
£105 Evereds Charitable Trust.
£105 Allied Supplies, Ltd.
£100 12s. 6d. From sale of gifts by W. R. Gibson.
£100 Lady Nadine Scarisbrick.
£100 M. Susman.
£100 Kelinwort Sons & Co. Ltd.
£50 Edwin T. Cato.
£50 Matheson & Co. Ltd.
£50 Sir Robert Renwick.
£50 Price & Pierce, Ltd.
£50 McCorquodale Group of Companies.
£50 Halford Cycle Co.

Appeal Covenants:

£1,000 p.a. for 10 years. Royal Exchange Assurance Co.
£714 p.a. for 7 years. Harry Joel Joel.
£500 p.a. for 7 years. Steel Company of Wales, Ltd.
£200 p.a. for 7 years. Monsanto Chemicals Ltd.
£150 p.a. for 7 years. South Durham Steel and Iron Co.
£100 p.a. for 10 years. The Rt. Hon. Lord Kindersley, C.B.E., M.C.
£100 p.a. for 7 years. British Plaster Board (Holdings) Ltd.
£50 p.a. for 10 years. Erlangers, Ltd.

Department of Anaesthetics:

£750 Shell Research Development Co.
£100 p.a. for 7 years. G.D. Searle & Co. Ltd. (under Covenant.)

Donations towards the cost of furnishing the new Committee Rooms:

£150 British Orthopaedic Association.
£100 Association of Industrial Medical Officers.
£25 British Association of Physical Medicine.

CARDIAC SURGERY

SIR RUSSELL BROCK's Bradshaw Lecture of 1957 on *The Present position of cardiac surgery* is now available in blue cloth binding, price 6s. a copy, from the following booksellers :

Baillière, Tindall and Cox Ltd., 8, Henrietta Street, Covent Garden, W.C.2.
H. K. Lewis and Co. Ltd., 136, Gower Street, W.C.1.
Lloyd-Luke (Medical Books) Ltd., 49, Newman Street, W.1.

BINDING OF THE ANNALS

BINDING CASES ARE not provided for completed volumes of the ANNALS but the Editor can recommend the firm of Lovett, Bookbinders, 86, Plashet Grove, London, E.6, who will undertake the binding in buckram or leather to individual requirements at reasonable prices.

DIARY FOR MAY

Mon. 18		Whit. Monday, College closed.
Tues. 19	5.00	MR. H. C. KILLEY—The maxillary antrum in relation to dental surgery.
	6.15	MR. S. H. WASS—Osteomyelitis of the jaws.
Thur. 21	5.00	PROF. E. D. FARMER—Oral Ulcers.
	6.15	MR. B. W. FICKLING—Surgical correction of deformities of the jaws.
Fri. 22	5.00	THE RT. HON. LORD COHEN OF BIRKENHEAD Charles Tomes Lecture—Facial neuralgias.*
Tues. 26		Last day for nomination of candidates (L.D.S.) for election to the Board of Faculty of Dental Surgery.
	5.00	MR. B. E. D. COOKE—Fibro-osseous swelling of the jaws—I.
	6.15	PROF. R. B. LUCAS—Pathology of oral neoplasms—I.
Thur. 28	5.00	MR. B. E. D. COOKE—Fibro-osseous swelling of the jaws—II.
	6.15	PROF. R. B. LUCAS—Pathology of oral neoplasms—II.
Fri. 29	5.00	DR. B. ANSON—Lecture—Development and adult anatomy of the auditory ossicles in relation to certain problems in endaural surgery.*

DIARY FOR JUNE

Mon. 1		Basic Sciences Lectures and Demonstrations for Dental students begin.
Tues. 2	5.00	DR. J. C. HOUSTON—Blood diseases in relation to dentistry.
	6.15	DR. VICTOR GOLDMAN—General Anaesthesia—I.
Wed. 3		Primary F.R.C.S. Examination and Final L.D.S. Examination (Part I) begin.
Thur. 4	5.00	MR. N. L. ROWE—Soft tissue infections of the face and neck.
	6.15	DR. VICTOR GOLDMAN—General Anaesthesia—II.
Wed. 10		Final L.D.S. Examination (Part II) begins.
	2.30	Ceremony of Presentation of Diplomas.
Thur. 11		D.P.M. Examination (Part I) and D.P.H. Examination begin.
	2.00	Ordinary Council
Tues. 16		Names of candidates (L.D.S.) for election to the Board of Faculty of Dental Surgery announced.
Wed. 17		Primary F.F.A. Examination begins.
	5.00	Board of Faculty of Anaesthetists.
Thur. 18		Pre-Medical Examination D.L.O. Examination (Part I) and D.P.M. Examination (Part II) begin.
Fri. 19		Election of Fellows to the Board of Faculty of Dental Surgery. Dental Lectures and Clinical Conferences end.
Thur. 25		First Membership Examination and D.L.O. Examination (Part II) begin.
Tues. 30		Final Membership Examination begins.

*Not part of courses.

CONSERVATIVE AND EXTENSIVE RESECTION FOR CARCINOMA OF THE LUNG

Tudor Edwards Memorial Lecture delivered at the Royal College of Surgeons of England
on
8th April 1959
by

Sir Clement Price Thomas, K.C.V.O., F.R.C.S., Hon.F.A.C.S., Hon.F.R.C.S.I.
Surgeon, Westminster Hospital and Brompton Hospital

MR. PRESIDENT, I am indeed grateful to you and to the President of the Royal College of Physicians and both your Councils, for the honour you have done me in appointing me to deliver the Tudor Edwards Memorial Lecture.

I am especially pleased to have the opportunity to pay tribute to one to whom I owe so much, and with whom I worked so intimately and for so long, perhaps for a longer time than any other of his colleagues. Our association commenced when I became his house surgeon in 1921 and lasted until his death in 1946 at the comparatively early age of fifty-seven years. He died when at the height of his powers and at a time when he could have expected the rich rewards which inevitably would have crowned his labours.

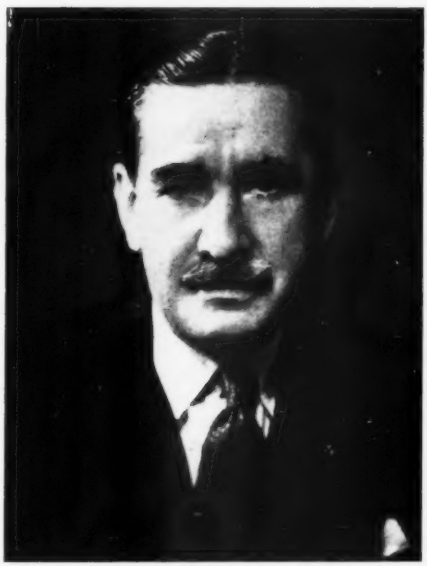


Fig. 1. Tudor Edwards.

He was born in Swansea in 1890, the son of a very successful draper, William Edwards. He was educated at Mill Hill School, of which he is one of their distinguished alumni. Later he went to St. John's College, Cambridge, whence he came to London to the Middlesex Hospital. It was here, during his formative years, that he came under the surgical influence of Bland Sutton and Gordon Taylor, and medically under that of R. A. Young, both the latter two we rejoice to have still with us; their influence, without doubt, did a great deal to mould his future outlook on and approach to medicine as a whole. At a later date, R.A., now Sir Robert Young, was to provide the greatest stimulation and encouragement to him in his early years in thoracic surgery, in fact, without this help, many more years would have passed before his efforts could have come to fruition.

During the First World War, he served, first as a regimental Medical Officer in the Scottish Horse, then in the 8th Stationary Hospital, but very soon he was transferred to the 6th Casualty Clearing Station, where, it is perhaps true to say, his surgical career began.

On his return from the War, he became Resident Assistant Surgeon at St. George's, and in 1919, he was appointed as Assistant Surgeon to Westminster Hospital.

Even at this early stage in his career, his technical skill was fully recognised, and those in contact with him marked him out for a career of some distinction. It is interesting that at this time, his colleagues thought him distant and at times a little arrogant, and his manner continued to earn him this opinion from many of his contacts throughout his life. I am confident, however, that this was not an accurate assessment of the man. Tudor was essentially shy and very much of an introvert, with all the handicaps that connotes. He never showed any trace of emotion, and he gave the impression that he thought it bad form so to do. I think this preservation of an outward calm was in reality a great tax on him, and possibly was a contributory factor in his early demise. It was impossible to get to know him intimately, he was too shut away within himself for that, and I believe I am right in saying that his wife, to whom he was devoted, and who, in turn, devoted her whole life to his care and comfort, was the only one who understood and knew him completely.

He set himself high standards, and demanded the same from those with whom he worked. To obtain his confidence was a difficult task, but, once gained, he was prepared to stand by that person in all circumstances. Forfeiture of his confidence however, meant, almost invariably, that it was never regained.

I first met Tudor when he came to Westminster as an Assistant Surgeon in 1919. At this time, his chief interest was urology; in fact, he introduced to our hospital modern urological procedures and, certainly for the first few years, this remained his chief interest.

In 1922, he was appointed as a Surgeon to Brompton Hospital, and it was then that he proceeded to lay the foundations of the work that was to bring him national and international fame.

He immediately paid a visit to the continent to see what other people were doing in the field of thoracic surgery and returned determined to exploit the challenge and opportunity which presented itself. Like Gask and Roberts, his interest in the surgery of the chest had been stimulated by his experience in a casualty clearing station in France, and this interest was paramount with him throughout his life.

His teaching was more by example than precept ; as a lecturer, he was apt to be uninspiring ; even as students, we always felt that he was even more pleased than we were when the lecture came to an end ; he spoke in a flat monotone, and it was almost unheard of that a jocular remark would enliven his discourse. I do not wish to imply that his method of teaching was inffective, far from it, one only has to consider the careers of the many thoracic surgeons here and abroad who sat at his feet which give such ample evidence of its efficacy.

He was at his best in the outpatient department and in the theatre, especially so with an inquisitive audience.

In the theatre, he rejoiced in the challenge of a difficult situation, and was to be seen at his best when facing some accidental happening. At this time, he was cool and collected, and, what is more, communicated his confidence to those about him. It should be fully appreciated that, at this time, there were no rules for many of the situations which had to be faced, and no previous experience on which to call.

He was a courageous surgeon ; had he not been, progress would have been very limited, for at this time the great advances in both radiology and anaesthesia, which were to come, had not been made, so that many of the interventions were done *secundum artem*. Tudor, however, was ready to use all methods as they arrived which would lead to success. However, it is interesting to recollect that the introduction of the tourniquet method of lobectomy and pneumonectomy by Shenstone, who incidentally gave the first of these lectures, delayed the general adoption of lobectomy by individual dissection of the hilar structure by many years ; this, despite the fact that in 1927 Tudor did his first lobectomy for bronchiectasis by individual dissection. Interestingly enough, Morriston Davies, who, I am glad to say, is still hale and hearty, did a lobectomy for carcinoma of the lung by the individual technique in 1914, which I believe to be the first recorded operation of this type for cancer of the lung.

One of Tudor Edwards' most valuable contributions to the progress of thoracic surgery in this country was the time he devoted to lecturing on his subject throughout the country, and his contributions to the literature of the subject. He contributed no less than thirty-four articles on a varied range of subjects, the last being when he was serving as the first

President of the Thoracic Society of Great Britain and Ireland. This Society was formed at his instigation to serve all those who have an interest in diseases of the chest, however remote, anatomists, physiologists, physicians, surgeons, pathologists and anaesthetists. This close relationship of all interests has been of inestimable value to this branch of study, and I believe it has been of value in the general field of medicine in pointing out the value of drawing the various arms of our profession into a closer relationship.

I have spoken of Tudor as a courageous surgeon : he was also a man of great courage. Few fully realise the physical handicap under which he laboured for at least the last ten years of his life. The manner of his passing could be forecast, for at least that length of time, before its happening. His high blood pressure and intermittent attacks of fibrillation were the premonitory symptoms, the significance of which he fully appreciated. After his first coronary occlusion, it was my task to try to make him take life more easily, but no, a life filled to the full was his only concern : that, rather than a longer one of curtailed activity. During the last seven years, with the exception of the times he spent in bed with an attack, I never heard him rail against his fate, and the uninitiated were quite unaware that he had ever had an illness. It is not given to everyone to face adversity in this wise, and one can only hope that, faced by such a fate, one would be given sufficient inward grace to meet it with as great fortitude.

Here then are the bare facts about a man to whom I owed and still owe a great debt of gratitude, a man one could not help admiring and respecting for his courage, fixity of purpose and integrity. He was too distant to command a warm affection, but this was compensated for by the deep regard with which he was held. Finally, in remembering him in this eponymous lecture, we do him honour for his life and the invaluable service he gave to his time and our generation.

I was at first uncertain as to how I could most fittingly in this lecture commemmorate the interests of my late colleague, in view of their catholicity. I have decided on carcinoma of the lung, a subject perhaps lying closest to his heart, for it was the subject of his address as President of the Thoracic Society, and was published in the first number of the first volume of Thorax, only eight months before his death, and was in fact his last publication.

The material on which his article was based is for practical purposes almost identical with my own material for the same period of time. I quote my own material because I shall have occasion later to consider these results in relationship with those of a later date. All the figures quoted in this communication are of patients operated upon personally, in order to exclude as many variables as possible. I apologise beforehand for inflicting on you a series of statistical tables, as I am fully aware that

statistics are only of real value to the person who compiles them, for he alone fully knows their true significance. Yet it is important that we should keep records of our patients, for it is only in this way that we can intelligently assess the value of what we are doing.

The results of patients operated upon from 1935-1945 are as follows :

TABLE I

Total No.	115		
Resections	69	ED = 14	(20 per cent.)
Thoracotomies	46 (41 per cent.)	ED = 12	(20 per cent.)
Pneumonectomies	64	ED = 13	(20 per cent.)
Five year survivals	17		(26 per cent.)
Lobectomies	5	ED = 1	(20 per cent.)
Five year survivals	1		

These figures are self-explanatory, it will be appreciated that the numbers are small and are only of value in assessing general trends. There are, however, three sets of figures, to which attention should be drawn ; firstly, that the thoracotomy rate in this group is 41 per cent. ; secondly, the early mortality rate, by which is meant those patients who die in hospital, irrespective of the length of time following the operation, the figure in this group is 20 per cent. for both types of resection ; thirdly, the low percentage of lobectomies to pneumonectomies, less than 10 per cent., and lastly, that the five-year survival rate for lobectomy is just over 20 per cent.

Up to this time, with very few exceptions, resection was undertaken only when the growth was confined to the lung, and had not invaded any of the surrounding structures, and then usually the whole lung was removed.

Fortuitiously at first, in that one was placed in the situation that the operation had to be completed, the scope of the operation was extended, and, at a later date, certain conservative measures were introduced. With greater experience it seems from the results that such modifications have proved to be of value. It is of these modifications of the standard operation that I wish to speak.

The background of my report is formed by the total number of patients submitted to operation since 1935 up to the end of 1958, the details of which are as follows :

TABLE II

Submitted to operation	826		
Resections	582	ED = 84	(14 per cent.)
Operable Cases	419	ED = 49	(11 per cent.)
Resectable Cases	163	ED = 35	(21 per cent.)
Thoracotomies	244 (29 per cent.)	ED = 30	(12 per cent.)

These figures show clearly that the overall mortality has been reduced almost by a third, despite the fact that the percentage of thoracotomies has decreased by just over 10 per cent. in other words, 70 per cent. of all

the cases submitted to operation have been resected, whereas in the earlier period only 60 per cent. were so treated, and in the last five years, 78 per cent. of the cases have been resected.

This steady increase in the resection rate has been due, not to a more limited selection of patients, but to a widening of our indications for resection, once the chest has been opened. In fact, our indications before operation have been widened, in that patients are now accepted of more advanced age, the oldest in the series being seventy-eight years; also patients with relatively poor respiratory reserve and those with various stigmata of inoperability, as judged by normal standards.

The term operable is used to indicate those operations in which only the lung, or part thereof, with the lymphatic field, has been removed; the term resectable is reserved for those in which the disease has extended from the lung into some structure, a portion of which has been removed with the lung, and it is this group, in the first place, that I wish to consider as constituting the cases submitted to the more extensive resection. It will be noted that the early mortality of that of the latter is almost double that of the former.

In attempting to assess the value of the more extensive procedures, I have chosen, for the sake of completeness, to analyse the records of all those patients who were submitted to operation before the beginning of 1954—these are shown in the following table.

TABLE III

PATIENTS SUBMITTED TO OPERATION FROM 1935 TO 1953 INCLUSIVE

Total No.	422		
Resections	279	ED = 44 (16 per cent.)	
Operable cases	219	ED = 25 (11 per cent.)	
Resectable cases	60	ED = 18 (30 per cent.)	
Operable five-year survivals	73	(33 per cent.)	Alive 53 Dead 20
Resectable five-year survivals	7	(11.6 per cent.)	Alive 4 Dead 3
Five-year survivals whole group	80	(28 per cent.)	

These figures show that the early mortality in the resectable group is practically three times greater than in the operable group, although, in the last five years, the disparity between the two groups is much lessened, and was in fact 19 per cent. in the resectable and 9 per cent. in the operable group. The other striking figure is the five year survival rate in the group I have deemed resectable. This for me was a gratifying surprise, for a great majority of the material in this group, without exaggeration, could be classified as inoperable. I find it impossible at the time of operation to forecast which individual patient will survive more than five years, even, for that matter, amongst those that fall into the operable group, and it seems to me that, from the patients' point of view, even at the expense of a greater risk, the more extensive procedure is justifiable on this score alone, not to mention the undoubtedly greater

comfort for the patient at the end, when the primary growth, which is not uncommonly associated with gross infection, has been removed.

I should like at this juncture to stress a few practical points about extensive resection which I think important.

Resection of the chest wall

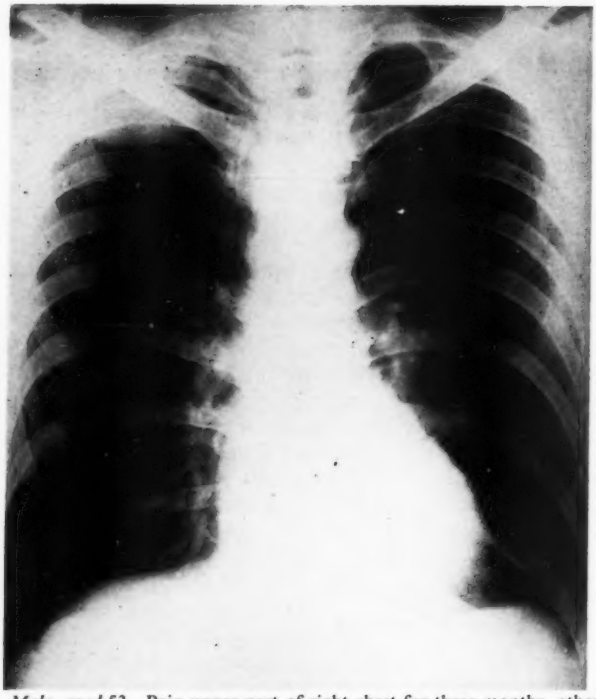
The chief value of this procedure, apart, of course, from the fact that it makes removal of the lung and tumour possible, is, in those cases in which, if they are left, the fully developed Pancoast syndrome develops; in certain cases, resection has been carried out when there is some evidence of involvement of part of the brachial plexus. When the sympathetic is involved, i.e., in the presence of a Horner's syndrome, it usually means that the vertebral bodies are involved also, and resection cannot be undertaken satisfactorily. Closure of the defect in these cases can be achieved, if the mediastinal pleura is not involved, by dissecting this up with the mediastinal fascia and sewing its upper cut margin to the edge of the chest wall defect. Lower defects in the chest wall, if large, can be closed with tantalum gauze, and, at the base, by attachment of the diaphragm to the upper margin of the defect.

Excision of portions of diaphragm

Closure of the resulting defect is usually easy: the defect is usually posterior and, when it is large, the margin of the diaphragmatic defect can be sewn to the chest wall higher up; it may be necessary to resect portions of one or more of the lower ribs in order to allow the chest wall to sink forwards to reach the diaphragmatic margin.

Excision of pericardium

The pericardium, I suspect because it is avascular, acts as a barrier to easy extension of the growth, and its excision is a perfectly rational procedure, provided the growth has not erupted into the pericardium, by which time the inner aspect of the pericardium will have been seeded with growth when surgery will be of no avail. The remaining defect normally should be left open. Only on the left side, and then only when the defect is large enough to allow the ventricles to dislocate from the sac, should the defect be closed; this may be done, as in one case by using a particularly large paracardial pad of fat, or by using a free pleural graft. Failing this, the patient should be nursed on the right side until the ventricles are fixed by adhesions into the pericardial sac; dislocation of the ventricles will most probably lead to ventricular fibrillation, which, if uncorrected, will rapidly lead to the patient's death. Under no circumstances should the pericardial edges be sewn together following excision of any part for, by doing so, the volume of the pericardial sac is reduced and may lead to tamponade, which, in the elderly, may be too great a burden, even though the degree of constriction may be small.



C.W. Male, aged 53. Pain upper part of right chest for three months, otherwise no respiratory symptoms. Latterly pain constant and running down inner side of right arm.

Fig. 2. Shows tumour mass right upper chest involving 1st and 2nd ribs. 19*th April*, 1955. *Right upper lobectomy* with resection of whole of 1st and 2nd ribs and portions of 3rd, 4th and 5th ribs, with reconstitution of part of chest.

Fig. 4. Shows right upper lobe with portion of chest wall attached.

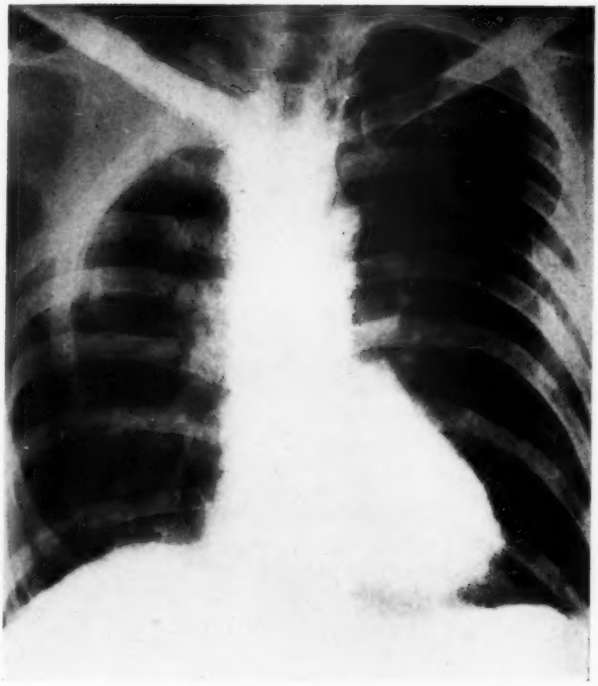


Fig. 3. X-ray following this type of operation.

Fig. 5. Shows tumour transected, showing bulging of extrathoracic portion of the tumour.

Patient survived only five months, dying from liver metastases, but pain was completely relieved.

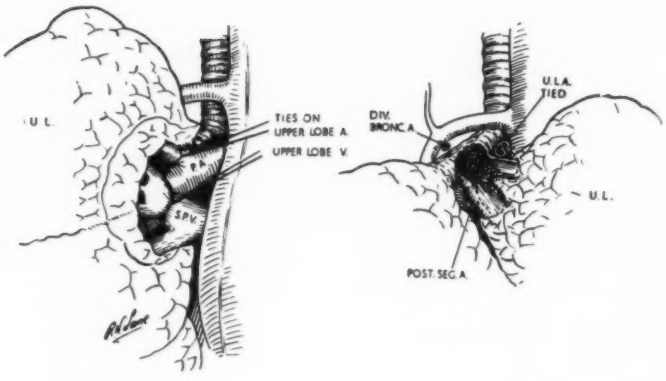


Fig. 6

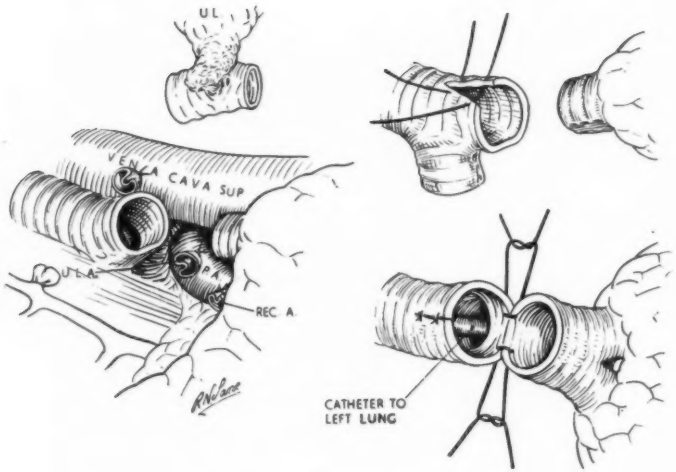


Fig. 7

Figs. 6 and 7 show diagramatically steps in sleeve resection of the main bronchus with the upper lobe, in this case on the right side. The stump of the main bronchus is too long for the operation when done on the right side, but would be quite suitable for a left-sided operation. The wedge shaped area excised in the bronchus is sometimes used to reduce the size of its lumen, but most commonly the lumen of both ends can be adjusted by suturing. The diagrams otherwise are self-explanatory.

Excision of the atrial wall

This is a safe procedure. Normally, when a resection for a carcinoma is being carried out, the venous return from the lungs to the left atrium should be controlled as early as possible, for there can be no doubt that manipulation of the tumour must lead to a greater risk of dissemination ; this is supported by the recent work of Warren Cole and his associates. A study of the causes of death following lung resection for cancer, in deaths occurring in this series, also supports this view, for out of 215 late deaths, in which the cause of death was ascertained, thirty-three, that is 15 per cent. of them, were due to cerebral metastasis, and over half of them due to cancer in other areas. When the growth has involved the atrial wall, the ideal of early venous control cannot be achieved, it is most often impossible accurately to place the clamps until the bronchus and artery are divided, and secondly, there can be no doubt that transection of the atrial wall should be the last manoeuvre before the lung is removed ; in this way, the atrial defect can be sutured promptly and any risk of dislodging the clamp can be avoided.

Excision of portion of the superior vena cava

Involvement of this structure is occasionally the only hindrance to a satisfactory operation. Sometimes a portion only of the vein need be removed and this can be done without interrupting the venous return by using an embolectomy type of clamp.

The occasion arises, however, when complete transection is necessary. It is essential, under these circumstances, that an anastomosis be done immediately the resection has been carried out. It is a great temptation to delay the suturing until the lung is out of the way, especially so as the patient's condition under anaesthesia appears to be satisfactory ; this delay in one case, without doubt, led to the patient's death from cerebral anoxia. In one other patient in whom the blood flow was arrested for just over fifteen minutes, the patient made a normal recovery, but there were fine skin petechiae over the chest wall and upper arms. Obviously a patient can accommodate to a caval obstruction of gradual onset such as occurs from the pressure of a growth, but an acute one of any length of time may lead to a fatality or serious disability.

Oesophagus

Gross involvement of the oesophagus is probably outside the pale of intervention. The type of case when resection is indicated, is usually discovered at operation and in a patient who has had no complaint of dysphagia.

Some surgeons routinely do a barium swallow, and tend to rule out operation in any patient in whom there is gross oesophageal distortion. This seems to me to be misleading, as not infrequently the distortion is due merely to the mass of the growth or of the inferior tracheo-bronchial

Fig. 8

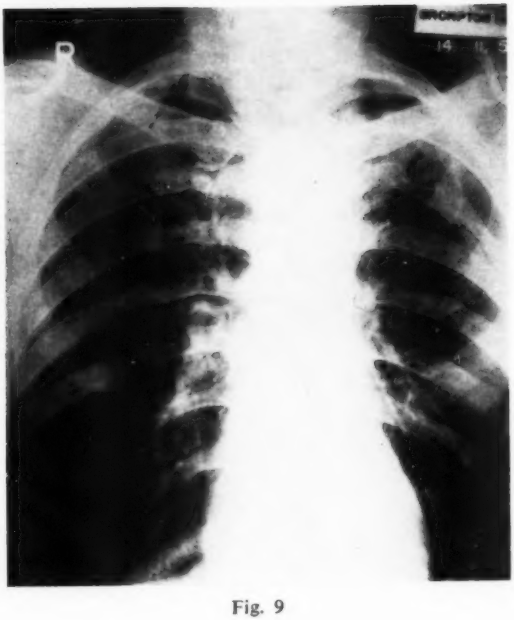


Fig. 9

Fig. 10

T. B. Male, aged 56. Presenting symptoms—breathlessness for five weeks, loss of appetite and weight. No haemoptysis and no other respiratory symptoms.

Fig. 8 shows shadowing in left mid zone which proved to be in upper lobe. 22*nd January*, 1958. *Bronchoscopy* shows a nodular stenosis of left upper lobe bronchus.

24*th January*, 1958. *Sleeve resection* of left main bronchus with upper lobe and sleeve of pulmonary artery, with anastomosis of pulmonary artery and bronchus.

Fig. 9. X-ray shows post-operative condition ten months following operation.

Fig. 10. Angiogram demonstrating the lower lobe artery patent and functioning.

Fig. 11 shows left upper lobe with main bronchus.

Fig. 12. Main and upper lobe bronchi cut across showing involvement of the orifice of the upper lobe bronchus.

glands, the oesophagus being merely displaced and the wall itself not being involved. If the patient has dysphagia and the barium swallow shows distortion or a block, then oesophagoscopy will confirm gross involvement which of itself indicates inoperability.

When involvement is found accidentally, then it is usually only one aspect of the oesphagus and often only the musculature is invaded, the mucosa being quite uninvolved. Excision of the affected area is simple.

Fig. 11

Fig. 12

Closure of the defect can be carried out, but it is essential to mobilise the oesophagus well above and below it to eliminate tension on the suture line.

To turn now to the more conservative approach. The following table is of the types of resections used up to the end of 1953.

TABLE IV

Pneumonectomies	246	ED = 41	(17 per cent.)
Five-year survivals	66	(27 per cent.)	
Lobectomies	33	ED = 2	(6 per cent.)
Five-year survivals	14	(39 per cent.)	

It will be seen that standard lobectomies form about 12 per cent. of the total, and that the five year survival rate is 39 per cent. This latter of itself is an index of the care with which the cases for lobectomy were chosen. This is in great contrast to the frequency of standard lobectomy in the last five years when 303 patients were submitted to resection and 126 of these had lobectomies, that is about 41 per cent.

This later increased use of lobectomy is a natural result of greater technical familiarity with the problem and also of the encouraging results achieved in the earlier period, combined with a desire to save as much of the patient's normally functioning lung tissue as possible.

The criteria for standard lobectomy, the operation in which the line of bronchial section is through the bronchus of the lobe which is being removed, are as follows. The tumour should be confined to the excised lobe, in that the other lobe or lobes are not involved, and the line of section should be so placed as to leave approximately a centimeter of apparently healthy bronchus between it and the level of macroscopic growth; we have found that, in the vast majority of cases, this ensured carrying out the resection through perfectly normal tissue; the lymphatic fields are cleared at the same time, in the case of the lower lobe, the inferior tracheo-bronchial region and the upper lobe, the paratracheal and most often the inferior tracheo-bronchial region as well; obviously in some cases the lobectomy falls into the resectable group, in that other structures are involved, and simultaneously removed.

The difficulty arose in carrying out a lobectomy in upper lobe tumours where the upper lobe bronchus itself was involved by the growth, in a patient who would not stand a pneumonectomy; under these circumstances, it is impossible to deal with this by standard methods.

Experience gained in the local resection of adenomas with the portion of the bronchial wall from which they grow, and the almost universally satisfactory technical results obtained gave sufficient encouragement to try to deal with this group of carcinomas. These were then treated by resecting, with the upper lobe, a sleeve of the main bronchus and anastomosing the two cut bronchial ends in order to restore the continuity of the bronchial tree. The following table shows the results of the series operated on up to the end of 1958.

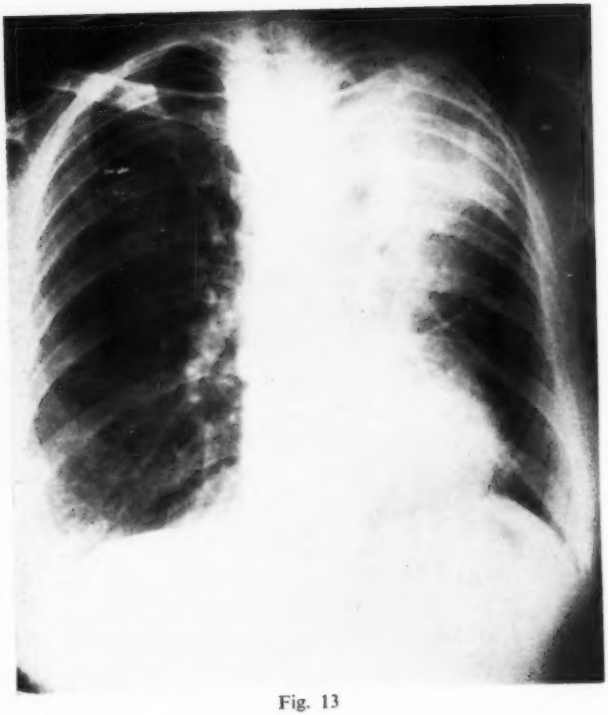


Fig. 13

Fig. 15

Fig. 14

E. A. Female, aged 60. Sole symptom pain in left upper chest present for nearly six months, involving left arm down the inner side to the elbow.

1*st October*, 1955. *Bronchoscopy* shows complete stenosis of left upper lobe bronchus by extrabronchial pressure. No obvious tumour visible. Biopsy negative.

11*th October*, 1955. Sleeve resection of left main bronchus with upper lobe and apical segment of lower lobe, and sleeve of pulmonary artery, also upper portion of infiltrated chest wall, with subsequent bronchial and arterial anastomosis. The operation entailed removal of the whole of the pleura covering the superior mediastinum, and, in consequence, reconstruction of the upper part of chest could not be carried out.

Fig. 13 shows pre-operative state.

Fig. 14 shows post-operative condition with high diaphragm.

Fig. 15 shows upper lobe and apical segment of lower lobe with overlying chest wall.

Fig. 16 shows mediastinal aspect of specimen with main bronchus indicated by glass rod and a length of pulmonary artery by probe.

Fig. 17. Transected specimen showing the tumour extending beyond the level of ribs and also the involved orifice of left upper lobe. Glass rod indicates pulmonary artery, the wall of which is also involved by growth.

Patient died nearly three years following operation from metastasis.

Fig. 16

TABLE V

LOBECTOMY WITH SLEEVE RESECTION OF THE MAIN BRONCHUS

No. of Cases .. .. 36 ED = 3 (8.3 per cent.)
Late Deaths 10

Length of survival of those alive

—1 year	1 year	2 years	3 years	4 years
7	4	8	2	2

Survival time of late deaths

—1 year	1 year	2 years
6	2	2

Fig. 17

These figures are small, but together with the patients dealt with in this manner by two of my junior colleagues, the number now reaches over 120.

The operation can be either elective or imperative. By elective, we mean that the operation can be carried out by this technique, if, at the time of operation, circumstances warrant it, but if the conservative procedure is not possible, then pneumonectomy can be undertaken without undue risk to the patient.

An imperative operation means that only a sleeve resection is warrantable, on the score of the poor cardiorespiratory reserve of the patient, and if this procedure is not possible, then the operation should be abandoned, as a pneumonectomy would be too dangerous. It has only rarely happened that the operation has had to be abandoned but, early in the series, a pneumonectomy was performed with a fatal result, when the conservative operation failed; consequently when the sleeve resection is imperative, an exploration which includes isolation of the vascular and bronchial elements is carried out before any irrevocable step such as ligation and division of vessels is undertaken; it is wise to clamp the pulmonary vein after it has been isolated until the feasibility of the operation is determined.

Sleeve resection, as with standard lobectomy, can be enlarged to include portions of other structures, chest wall and pulmonary artery being the most common element and, more rarely, pericardium.

Resection of portion of the pulmonary artery is most common on the left side, where the artery arches around the upper part of the upper lobe bronchus. Sometimes only a segment of the lumen of the artery has to be sacrificed, at other times a whole segment of the artery has to be resected. During the repair, the bronchial suture should be completed first, and finally the arterial suture, otherwise there is a great risk of tearing of the arterial suture line. Incidentally, removal of the main bronchus gives as complete access to the inferior tracheobronchial angle as does a pneumonectomy.

The figures for standard lobectomy performed during the same period for comparison with those for sleeve resection during the same period are as follows:

LOBECTOMIES—1954-58 (INCLUSIVE)

No. of Cases .. .. 126 ED = 12 (9.5 per cent.)

Length of survival of those cases

—1 year	1 year	2 years	3 years	4 years
36	15	10	9	4

Those of late deaths

—1 year	1 year	2 years	3 years	4 years
22	14	2	2	—

The long-term results of the operation of lobectomy with sleeve resection of the main bronchus cannot yet be assessed, but the survival rates compare very favourably with those for standard lobectomy for the same period but, of course, the figures are much smaller for sleeve resection than for lobectomy.

We feel satisfied by our combined experience, that this is a procedure

worthy of trial, and it certainly affords relief for a group of patients who perforce heretofore have had to be deemed hopeless.

In conclusion, I would like to summarise in this way. Surgery offers no answer to the problem of cancer, but it is at the present time the best form of treatment for the patient suffering from cancer of the lung; and, until a better be found, there is every justification for extending our indications for surgery to include such extensions of the disease that are within the competence of removal, for none can judge at the time of operation which patient will or will not have a long term survival apparently free from disease. I would also like to put in a plea for conservatism, where this is rationally indicated, for, by doing so, we in effect extend the range of application of surgical relief.

APPOINTMENT OF FELLOWS AND MEMBERS TO CONSULTANT POSTS

I. W. WINCHESTER, M.CH., F.R.C.S.	Traumatic and Orthopaedic Surgeon to Whittington Hospital.
B. SCHWARTZ, M.D., M.R.C.S., D.P.H.	Dermatologist to Barnet General Hospital.
J. M. DAVIS, M.CHIR., F.R.C.S.	General Surgeon to Whittington Hospital.
D. L. B. FARLEY, M.B., B.S., F.R.C.S.	Surgeon to Royal Northern and Highlands General Hospitals.
D. I. STIRK, F.R.C.S.	Consultant Surgeon to North Devon Group of Hospitals.
I. S. JONES, M.A., M.B., F.R.C.S.	Consultant General Surgeon to the Plymouth Clinical area.

The Editor is always glad to receive details of new appointments obtained by Fellows and Members, either through the Hospital Boards or direct.

RECENT OVERSEAS VISITORS TO THE COLLEGE

RECENT OVERSEAS VISITORS to the College have included Dr. E. D. Ahern of Brisbane and Dr. John H. Gibbon of Philadelphia who were admitted to the Honorary Fellowship of the College during the meeting of the Council in May: Professor J. H. Louw of Cape Town, who delivered a Moynihan Lecture in April, Mr. and Mrs. Susman of Sydney and Mr. and Mrs. Matheson of Montreal, who attended the monthly dinner in May and Professor R. B. Kerr of Vancouver.

ANATOMICAL MUSEUM

THE SPECIAL DISPLAY for the month of June consists of a series of photographs showing the architectural history of the museum.

LOCAL FACTORS IN HEALING OF THE ALVEOLAR TISSUES

Charles Tomes Lecture delivered at the Royal College of Surgeons of England on 10th September 1958 by

Professor H. G. Radden, M.Sc. D.D.Sc., F.D.S.R.C.S., F.D.S.R.C.S.(Ed.)
Dean of the Turner Dental School, University of Manchester

INTRODUCTION

THE REMOVAL OF teeth, whether by accident or design, and the resultant disability, is probably the oldest and most common dental problem of mankind. It is remarkable, therefore, that whilst early historical writings contain many references to diseases of the teeth and gums and their treatment, one rarely encounters descriptions of tooth removal. In these rare instances, however, the reader cannot fail to be impressed with the knowledge of basic principles displayed, some of which I fear are not always applied today.

In 300 B.C. Aristotle stressed the need to search for and remove pieces of bony alveolus fractured during the removal of teeth.

Later, the Arabians in the Middle Ages, following the example set by their Greek and Roman predecessors, showed a certain reluctance to the bloody operation of extracting teeth. In the case of a very troublesome tooth, when all else failed, they resorted to medicaments containing arsenic which, as you may well know from your reading, and not, I trust, from your practice, prove just as effective in the removal of teeth.

Today, the loss of teeth may well become the most frustrating problem of the dentist called upon to fit dentures to a mouth deficient in alveolar bone—a problem which he will need to overcome if his relationship with his patient is to be on an amicable basis and not one which deteriorates into a series of unfriendly daily skirmishes.

Inadequate alveolar bone may be the result of long standing untreated parodontal disease, too radical surgery during extractions, or come about progressively with age during which the process may be accelerated by the presence of ill-fitting dentures.

But since the fitting of dentures to such mouths is an ever-recurring problem which shows no sign of abatement it was thought a study of the processes taking place following the removal of teeth might lead to measures for controlling bone resorption or failing this to the development of methods which would facilitate the deposition of new bone.

The study of extraction wounds, however, is not new, for it was reported in some detail by Euler in 1923. Working on dogs he extracted teeth at intervals, with the object of studying sockets in varying stages of healing from three to sixty-three days.

Similar work was carried out by Meyer in 1924 and Szabo in 1927 ; the former also investigated the influence of foreign bodies and infection on

healing. Schram in 1929 and Claflin in 1936 studied the effects of surgical removal of the buccal alveolar bone and Versnel in 1953 investigated the effects of haemostatics and antibiotics on the rate of healing.

Steinhardt in 1932 carried out a histological investigation post mortem on humans in three cases with a history of extractions prior to death. Christopher (1942) investigated material obtained from healing sockets in humans, and Mangos in 1941 carried out a complete histological study in normal adult humans and showed that the healing process, except for taking longer to complete, follows the same pattern as in the dog.

Observations have also been made on the sheep by Harrison in 1943, on the rat by Glickman, *et al.* (1947), investigating the influence of retained roots and bone fragments on the rate of healing and by Huebsch, *et al.* (1952), to establish the normal, prior to an investigation of the effects of dietary changes on the healing process in the rat.

Only last year at the British Dental Association's Annual Conference (1957), Simpson, reporting on the "Healing of Extraction Wounds" in Rhesus Macacus monkeys, made special mention of the part played by the epithelium.

Tooth removal with forceps is brought about by the application of force in a series of movements, variously described as thrusting, rotating, levering. These movements, although largely developed by trial and error, should logically be predetermined as to their nature, direction and sequence from a knowledge of root structure and the alveolus of the particular tooth involved. Designed as they are to remove the tooth *in toto*, the applied forces result in a stripping of epithelium from the tooth and a tearing of the periodontal fibres in some part of their length ; this latter depending no doubt on the nature and direction of the forces applied.

As well as extraction with forceps, however, there are other methods of removal of teeth with which you are all familiar and, associated with these, certain principles have come to be accepted as standard procedure. Many of these principles stem from clinical observations indicating that one particular method gives better results than another. For example, many dental surgeons consider that a modified or conservative alveolectomy following extraction of teeth, materially assists the healing process as well as permitting early insertion of dentures well tolerated by the patient ; whereas under different conditions, as with a straight extraction technique, early insertion of dentures may be quite impossible.

The present series of experiments, therefore, was designed to rationalise some of the techniques used in the surgery of the alveolus, and in an attempt to answer some at least of the many questions which any thinking dentist must have posed for himself at some stage of his career, and although at first glance the title of my address may suggest it will be academic, practically all of the substance you will find to have application to everyday dental practice.

Materials and methods

The Rhesus Macacus monkey, possessing as it does a dentition closely resembling that of man, was chosen for the requisite surgery, and in all twenty-seven monkeys, showing no clinical or radiographic evidence of systemic disease and with no caries or paradontal disorders, were utilised. Their average age, as computed from their dentitions and body weights, was approximately fifty-two months and all operations were performed on teeth of the permanent dentition. Prior to and during the period of the experiments they were maintained on a diet adequate in all essentials, and all animals showed increases in weight during this time.

Anaesthesia was induced with intravenous $2\frac{1}{2}$ per cent. sodium pentothal (36mgms. per kilo of body weight) and maintained with endotracheal nitrous oxide and oxygen, with complete packing of the oro-pharynx. The oral cavity, lips and surrounds were then prepared with 1 per cent. Cetavlon (Cetramide) and the area draped with sterile linen. The operators then carried out the accepted preparation for aseptic surgery so that it could be claimed that the healing processes in all operations were unaffected by the presence of organisms not normally found in the monkey's mouth, and to ensure that extraction with forceps would serve as a true basis for comparison with the more prolonged surgical procedures where such surgical preparation is routine.

Operations were so timed to provide material at intervals from three to sixty-three days and the tissues were then prepared by routine histological methods and sectioned in series at 7 microns.

Perhaps at this stage I should refresh your memories regarding the teeth of the Rhesus Macacus monkey. You will remember it possesses a deciduous and permanent dentition similar to man, the same number of incisors, premolars and molars.

The teeth removed in the experiments were the upper laterals and the lower incisors and both the upper and lower premolars and some molars and their actual removal was accomplished utilising the following methods :

1. *Extraction with forceps* followed momentarily by digital compression of the soft tissues.

2. *Surgical Removal.* This consisted of reflection of mucoperiosteal flaps from the bone by incising the buccal and lingual gingival tissues around the necks of the two premolars to be removed and extending the buccal incision through the periosteum downwards, deeply into the buccal sulcus from two points, (*a*) between the first premolar and canine and (*b*) between the second premolar and the permanent molar and so as not to interfere with the gingival attachments on both the canine and molar and never less than 2mm. from the epithelial attachment to these teeth, and at such an angle in each case as to allow the flap subsequently to slide over and completely cover the sockets remaining after removal

Fig. 1. Flap reflection.

Fig. 2. Flap replacement.

of the premolars (Fig. 1). To enable this to be done, the buccal flap as outlined was elevated from the bone right down into the sulcus where the periosteum only was incised horizontally.

Sufficient alveolar bone was then removed with burs from the crests of the ridge to enable the premolars to be readily elevated from their sockets. The prominent portions of the bony alveolus were then removed and the height overall reduced and smoothed with Rongeurs forceps and burs prior to complete excision of the papillae from both lingual and buccal flaps. The buccal flap was then carried across the open sockets and its cut edge placed and held in position with interrupted sutures against the same edge of the lingual flap (Fig. 2).

A further series of flap reflections included the whole of the gingival tissues of the remaining teeth instead of avoiding them.

The complete series then provided material of surgical extractions and two methods of flap reflection to which I will refer later.

3. *Extraction with forceps and the performance of two types of alveolectomy.*

(*a*) Elevation of mucoperiosteal flap. Removal of the cortical buccal bone, and replacement of the flap with suturing ; and

(*b*) removal of the interradicular bone and collapse of cortical plate with suturing—interseptal alveolectomy.

Results

There will be no *need* to tell you that an extracted tooth always brings away with it some of the enveloping tissues, but since this may influence the subsequent behaviour of the remaining tissues, it may be as well first examine what is actually removed with the tooth when it is extracted with forceps.

Histological section of such teeth shows that they often have attached to them epithelium, periodontal membrane or even bone, and immediately after the removal of a tooth, therefore, one may expect to find exposed in a socket :

1. Lacerated epithelium,
2. areas of periodontal membrane,
3. areas of cortical bone denuded of periodontal membrane, and
4. areas of cancellous bone,

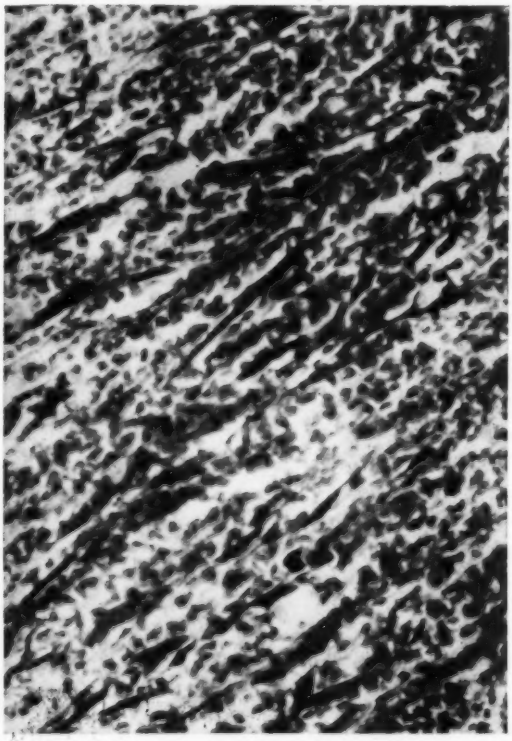


Fig. 3. Fibroblasts and young capillaries growing into blood clot at three days. × 340.

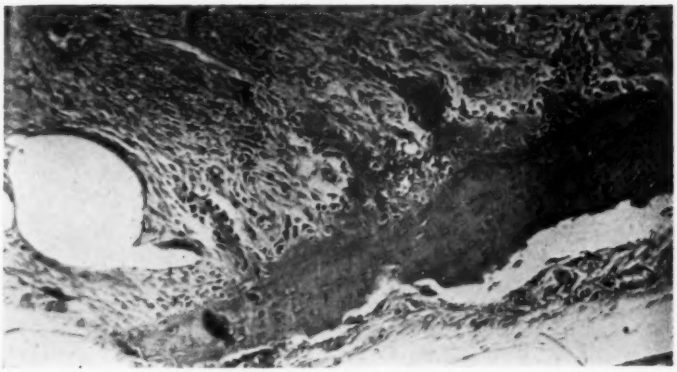


Fig. 4. Osteoid tissue growing from cancellous bone at base of socket from six to seven days. × 90.

all or any of which may be relatively normal or seriously damaged by trauma and infection.

No doubt you will be familiar with the main details of healing in the alveolus, but I must ask you to be patient whilst I very quickly describe our findings of uncomplicated healing when teeth were carefully removed with forceps and no further attention given to either hard or soft tissues. I do not propose to give complete details, but rather to point out the salient features and the times at which they are apparent, and then, utilising these results as a basis, compare and contrast the results obtained by the other methods I have mentioned.

Twenty-four hours after extraction the socket is filled with blood clot and fibrin strands, with granular leucocytes covering the surface. The interdental papillae have contracted in towards the alveolar crests and blood vessels immediately surrounding the wound are widely dilated.

At three days reparative processes have commenced with proliferation of the basal layer of epithelial cells, and ingrowth of young fibroblasts and budding capillaries into the clot (Fig. 3) and by *four days* much of the remaining periodontal membrane shows signs of degeneration.

At six to seven days small areas of osteoid tissue are seen growing from existing cancellous bone in the deeper portions of the socket (Fig. 4) and osteoclasts are present on the crests of the interdental septa.

At ten days there is a thin epithelial layer of four to six cells in thickness across the wound but centrally in the socket some blood clot still remains (Fig. 5). Osteoblasts are absent where inactive periodontal membrane still exists. Osteoid tissue extends as projections from all other parts of the socket wall but it is most advanced in the apical third.

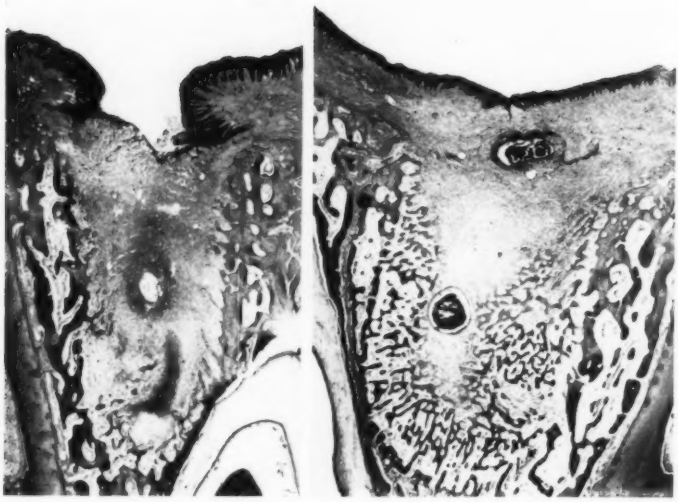


Fig. 5. Fig. 6.

Fig. 5. Thin epithelial layer over the wound at ten days. × 7.

Fig. 6. Osteoid tissue forming right up to the crests of the alveolus at fifteen to sixteen days. × 7.

By fifteen to sixteen days the epithelium has become keratinised and developed rete pegs and although inflammatory cells are reduced in number and the connective tissues immediately beneath appear more mature and less vascular, the fibres are still irregularly arranged. Osteoid tissue is now forming right up to the crests of the interdental septa, the apical third of the socket is filled with new bone (Fig. 6) and the outline of the socket in this region is often difficult to determine. Occasionally, even at this late stage, some blood clot may persist.

At twenty-seven days the socket is almost filled with new bony trabeculae and vascular connective tissues, but as late as *forty-seven days* new osteoid tissue may still be being laid down on the surface of the original socket (Fig. 7). Deeper in the tissues there is now marked reduction of vascular elements.

At sixty-three days the superficial trabeculae have combined to form an irregular surface between the two alveolar crests and in this region bundles of connective tissue fibres are grouped together to form what will be the new periosteum (Fig. 8).

Generally, it may be said of this series that it conforms to the pattern reported by other workers, both as to the time factor and the regeneration of the various elements. It is important to remember that the main source of new bone is from the cancellous areas of the old, and by comparison

the periodontal membrane and the periosteum contribute relatively little to the healing processes.

Bearing these things in mind, let us now turn to the results of the other series.

With the alveolectomy involving stripping of periosteum and removal of cortical bone, it will be immediately apparent that there is a lessened surface area of cancellous bone available for regenerative purposes and hence some slowing down of bony replacement seems inevitable, and this has indeed proved to be the case.

There is, however, in this series, ample mucoperiosteum to cover completely the reduced area of exposed bone, and so long as careful débridement is carried out and the flaps replaced, healing proceeds uneventfully. When these latter precautions are neglected there is always

Fig. 7. New osteoid tissue still forming at forty-seven days. × 10.

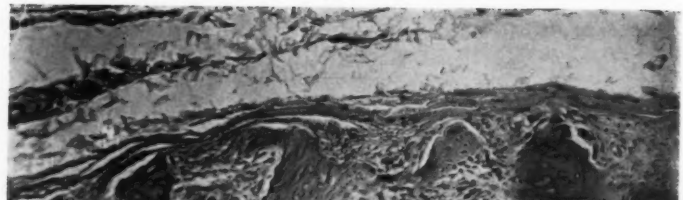


Fig. 8. Bundles of connective tissue fibres forming new periosteum at sixty-three days. × 100.

Fig. 9. Interseptal alveolectomy. Fracture of cortical plate at "A". × 7½.

delayed healing. In any event, by this method, return to normal bony architecture with the building of cortical plate lags behind the other methods employed. Whether the stimulus of a functional, tissue-borne denture would modify this result, we are not in a position to say, but it is a question which should be investigated.

In the series of interseptal alveolectomies with intact periosteum and collapse of cortical plate, the blood clot in the socket is minimal and, since there is no loss of inner cancellous bony surface, reconstruction commences early in what is a *reduced* socket. In addition, the bone comprising the alveolar crest, that portion so prone to become infected when divorced from periosteum, apparently receives sufficient stimulus from the operation as to provide early proliferation of the bone-forming elements and hence, by this method, bony reconstruction in the early stages is somewhat in advance of the other extractions (Fig. 9).

With the exception of those cases suffering loss of cortical bone, there comes a stage around the three to four weeks period in the other methods of extractions, in which there is really no difference in the healing processes and it could not be said one method was better than another. Indeed, by forty-seven days, in some instances it was difficult to tell which method of extraction had been utilised in the experiment.

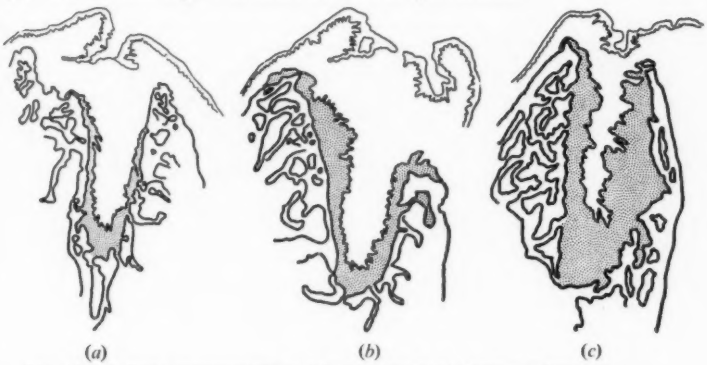
Briefly I can perhaps best compare the methods diagrammatically. Figures 10 (*a*), (*b*) and (*c*) and 11 (*a*), (*b*) and (*c*) are reproductions of camera lucida drawings of actual sections.

Let us first look at bone regeneration at thirteen days (Fig. 10 (*a*), (*b*) and (*c*)):

(*a*) With forceps extractions (the stippled area shows the new bone),

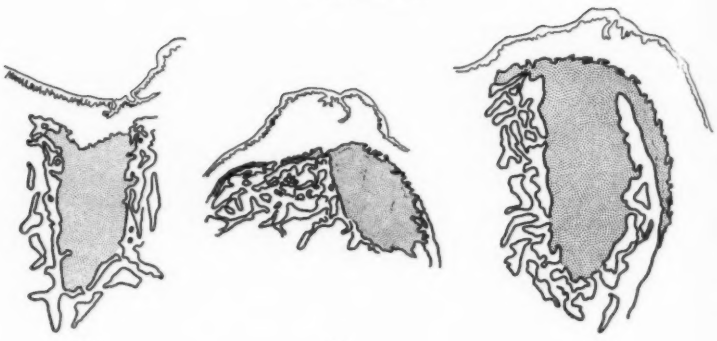
(*b*) where the cortical plate was removed, and

(*c*) where interseptal alveolectomy was performed.



(*a*) (*b*) (*c*)

Fig. 10. (*a*) Bone regeneration at thirteen days with forceps extraction.
(*b*) Bone regeneration at thirteen days with cortical plate removed.
(*c*) Bone regeneration at thirteen days with interseptal alveolectomy.



(*a*) (*b*) (*c*)

Fig. 11. (*a*) Bone regeneration at forty-seven days with forceps extraction.
(*b*) Bone regeneration at forty-seven days with cortical plate removed.
(*c*) Bone regeneration at forty-seven days with interseptal alveolectomy.

It shows that with the interseptal method bone regeneration is somewhat more advanced at thirteen days.

But by forty-seven days (Fig. 11 (*a*), (*b*) and (*c*)) except that the cortical plate is immature, i.e., the centre section, there is really little difference in the results.

Let us now consider in more detail the tissues taking part in the regenerative processes. First the connective tissues and bone, and then the epithelium.

1 (*a*) The periodontal membrane

In the case of forceps extraction where considerable force and manipulation is required, much of the periodontal membrane comes away with the tooth and the portion remaining behind is so damaged as to be unable to contribute anything to the regenerative process. Where it does survive, recovery is greatly retarded and proliferation of the connective tissue elements may not occur until six to seven days after the extraction. No doubt it is under such circumstances where dead and degenerating connective tissues provide a nidus for bacteria that dry sockets occur. Clinical evidence would support this thesis for I feel you will *all* agree that a dry socket is most prone to occur after a difficult and traumatic extraction.

Survival of the periodontal membrane most often occurs in the apical region, less frequently towards the crests of the bony alveolus and comparatively rarely in the middle third of the socket.

Within the socket there is always some alveolar bone completely denuded of periodontal membrane, but such areas are often the first to show new bony trabeculae, possibly because the lamina dura in such places is perforated by numerous nutrient canals. This may also explain why these tissues containing fewer collagen fibres come away with the

tooth, and why, in less vascular areas, there is more damage from manipulation before rupture and less capacity to regenerate.

As practising dentists our knowledge of the lamina dura is derived largely from X-ray pictures which, in the absence of pathology, show it as an almost continuous radio-opaque line around the tooth root. Under a microscope, however, it is really not cortical bone of a type seen on the surface of the mandible and it is, in fact, perforated by numerous nutrient canals (Fig. 7), especially in young persons. A little more attention to these X-rays prior to extractions in the middle-aged will be amply repaid in the avoidance of the unfortunate sequelae of traumatic extractions with forceps.

1 (*b*) Connective tissues of the alveolar crest

In the case of surgical extractions where freshened epithelial surfaces were placed and held in apposition, the connective tissues beneath showed an entirely different picture from those in the other series. At three days in the former instance there was a remarkable absence of granular leucocytes and the connective tissue elements on the crests of the reduced alveolus showed *no degenerative* changes but considerable activity (Fig. 12). This may be due partly to the absence of trauma in this operation, as

Fig. 12.

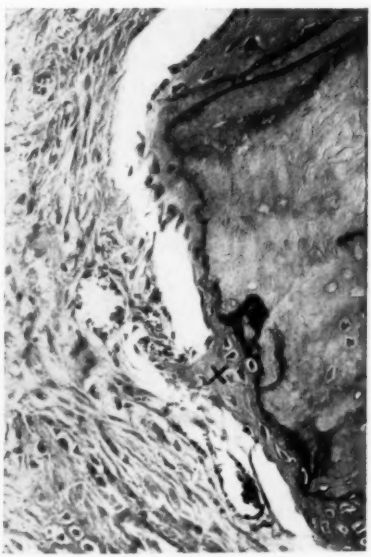


Fig. 13.

Fig. 12. Active connective tissue elements at " X " on the crest of the alveolus. × 90.

Fig. 13. New bone (X) being deposited on old bone in the socket. × 200.

compared with direct forceps extraction and the reduction of the alveolar crests exposing cancellous bone which is much more active in regeneration than cortical bone. It is noteworthy, however, that under similar bone surgery, but dissimilar soft tissue treatment, where the papillae were not removed, these tissues told a different story. In each instance, and despite what we thought was careful débridement, small pieces of bone were usually found in the tissues around the alveolar crests and over the mouth of the socket.

In *forceps* extractions and *surgical* removals where papillae were only placed in apposition, most of these bony pieces became infected and local disturbance to healing resulted, whereas with very careful flap replacement following excision of the papillae, they apparently did not become infected and, in many cases, were built into the framework of the new bone (Fig. 13). There is, of course, no need for me to remind you of the trouble such spicules may cause one's patient when they do become infected.

1 (*c*) The bone—ossification of socket

In the case of forceps extractions the first osteoid tissue appeared at six days as a proliferation from the cancellous bone of the apical region, whereas under the ideal conditions of surgical removal and complete closure, some of this tissue was just detectable at three to four days.

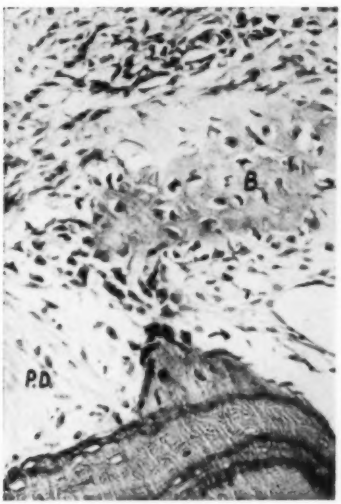


Fig. 14.

Fig. 15.

Fig. 14. Surviving periodontal membrane (PD) and new bony trabeculae (B) at thirteen days. × 175.

Fig. 15. Implanted bone. × 60.

In all the series the cancellous bony elements provided practically the whole of the new bone to fill the socket ; where the periodontal membrane survived it early provided a matrix in surgical extractions, and somewhat later in forceps extractions. It was, however, only converted into bone at a far later stage to those areas ossified from the medullary spaces. Here is a slide of a thirteen-day-old socket in which there is surviving periodontal membrane with *no* ossification and, alongside, new bony trabeculae (Fig. 14).

Large pieces of bone with attached periosteum

These are seen in cases of interseptal alveolectomy where there is relatively minor disturbance to environment and vascular supply. They play a very prominent part in the healing process by providing from their inner surfaces new bony trabeculae which rapidly fill the reduced socket space resulting from this operation (Fig. 9).

In other cases, fairly large pieces of bone with attached periosteum, in the absence of infection, when implanted deeply into sockets are readily accepted by the connective tissue elements and utilised as a base for deposition of new bone and do provide some of the cells necessary for this growth (Fig. 15). When infection is present it first involves the exposed surfaces of the cancellous bone, and only later affects the periosteal face of the bone, if at all, for in some cases the latter surface and the attached soft tissues survive.

Large pieces of bone without periosteum, although deeply implanted in the socket, usually degenerate and may become infected, and in any event are resorbed.

Smaller pieces of bone lying free in the blood clot, approximately at the level of the remaining alveolar crests, rarely survive, become infected and serve as an attraction for the epithelial elements which not only search out but also surround them, and would seem to be partly, if not wholly, responsible for their extrusion (Fig. 16).

In surgical extractions, despite syringing and careful cleansing of the wound on completion of the operation, study of histological sections showed considerable quantities of small bone particles produced by the bur and lodged in the mucoperiosteal flap. Only in rare instances did they initiate an inflammatory response in this site. No doubt this is explained by the fact that the particles were sterile in the first instance and remained so by virtue of their position, well away from the wound opening. The very nature and size of the particles allowing ready access of tissue fluids to all parts would no doubt determine whether they would remain viable.

Epithelial tissues

Let us now look more closely at the epithelial tissues. We have already seen that, following operation, the basal cells of the stratified squamous layer proliferate in the third day across the surface of the exposed connective tissues immediately beneath the mat of polymorphonuclear leucocytes.

Fig. 16.

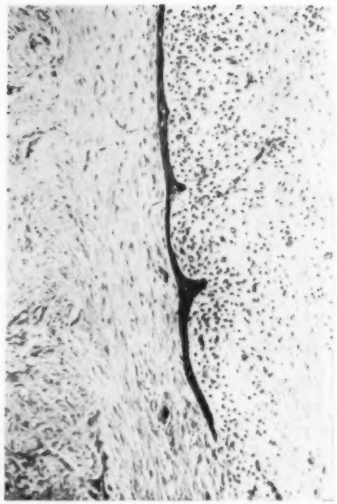


Fig. 17.

Fig. 16. Epithelial strand enclosing bony fragments. × 70.
Fig. 17. Epithelial strand traversing connective tissues. × 100.

Harris (1955) explains this by saying that

> " Cells, whether connective tissue or epithelial, are stimulated to multiply when normal spatial relationship between them is disturbed, and cease multiplication when the normal relationship is restored."

This would apparently explain the present behaviour for it would seem designed to re-establish normal spatial relationships of epithelium to connective tissues. No doubt, also, it is in a region *optimal* as to nourishment and oxygen tension for growth of these epithelial tissues.

Harris's statement, however, does not explain such a condition as shown in this slide where long tongues of epithelial tissue traverse in depth fairly normal connective tissues (Fig. 17). Surely in this case other influences must be at work. Whilst the pathologist explains this phenomenon as chemotaxis, Bier (1917) is a little more specific and says that cell proliferation is due to what he calls " wound hormones "—probably the intermediate and end products of protein degradation—and I think no-one will deny that in an extraction wound such hormones will be plentiful indeed.

This purposeful action of the epithelium eventually results in the extrusion from the tissues of the substance to which the cells have been attracted, be it a foreign body, as occurs for example with a zinc oxide dressing (Fig. 18) or some tissue which has promoted the same response, whether from degenerative change or infection, or possibly both these

influences. Simpson and other workers have drawn attention to this, with regard to bone. Extrusion, by the way, may mean actual expulsion from the tissues or encapsulation, and in both senses the ultimate result may not be dissimilar.

Florey (1958) draws attention to the fact that extracts of normal tissues, both embryo and adult, and of inflammatory and autolysed tissues as well as protein degradation products, all promote growth of this kind.

What is perhaps more remarkable is a directional influence exerted on these cells, perhaps readily understood on the surface of granulation tissue as I suggested, because of the establishment of normal spatial relationships to the underlying connective tissue, but more difficult to understand at a gingival attachment where some relatively minor infection sets off strands of epithelial cells, not only along the root but into the underlying connective tissues.

There is another point—epithelial cells do not stop when they establish relationship with a piece of bone or tooth, but run along its surface, sometimes right around it (Fig. 19). Can this be explained by the establishment of spatial relationship?

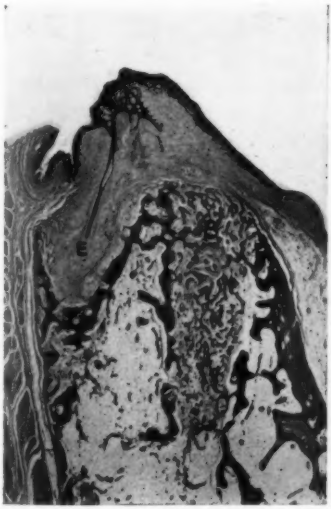


Fig. 18.

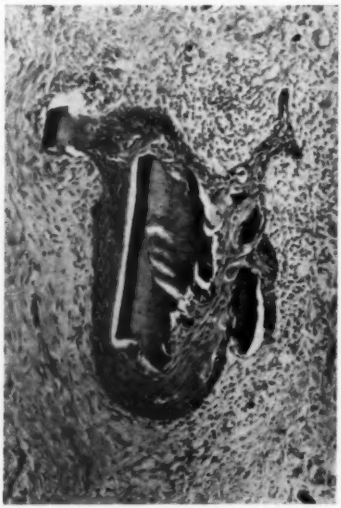


Fig. 19.

Fig. 18. Transverse section of premolar socket at forty-seven days showing epithelial strand (E) to zinc oxide implant in buccal socket (zinc oxide not present in this section) and lingual root socket (B) completely filled with new bone. × 7.

Fig. 19. Cementum and dentine surrounded by epithelium. × 110.

There are other epithelial cells about a healing socket, however. What has happened to the remains of the Sheath of Hertwig, the Rests of Malassez ?

Why have not some of these cells been activated by the " wound hormones " ? In the sections of teeth extracted with forceps it was noticeable that these epithelial cells were often removed with remnants of the periodontal membrane, for they are situated close to the root, and it is understandable that those remaining in the socket may be so damaged as to be unable to proliferate and, indeed, despite careful search, we did not find any of these cells remaining in the sockets. In the case of surgical removals, however, where much of the periodontal membrane remained in good condition, we *did* find epithelial cell rests in a similar condition, but we *were* unable to discover any signs of proliferation.

Where disturbed and delayed healing occurred, strands of epithelium were often apparent in the connective tissues up to forty-seven days following extractions and it would seem from our observations that such elements may be the forerunners of cyst formation. In order to increase our knowledge of this aspect we therefore implanted small pieces of oral epithelium under the mucosa of the alveolus ; in all instances these elements formed cysts from degeneration of the central cells of the implant.

Unfortunately, time will only allow me to make one further observation with respect to these implants. *We* feel it is important, however, for it clearly shows the effects epithelial elements may have on the approximating connective tissues.

Here then is an epithelial implant of forty-seven days' duration, and here it is stained with Gomori's Aldehyde Fuchsin (Fig. 20), and clearly showing how the elastic fibres have been organised into what appears to be layers around the implant. No such arrangement could be found under normal environment.

This section of the work, however, is at present incomplete and I only mention it in passing. It is hoped to report it in detail at a later date.

Reflection of mucoperiosteal flaps

Although the method of reflection of the mucoperiosteal flap from a tooth to be removed is not important, it is of considerable significance when the tooth is to be retained, for it will not be denied that the condition of the soft tissues around a tooth is so often the main determinant in the life span of that tooth. This has been forcibly brought home to us following the removal from the palate of the impacted canine ; we have carried out in the Manchester Dental Hospital some 300 operations of this nature in the last four years so there has been ample opportunity to observe the results.

In our experience, the great majority of these cases present as a canine lying obliquely in the palate and impacted against either the central or

Fig. 20. Elastic fibres surrounding cystic epithelial implant at forty-seven days : ("E" Epithelium ; "C" Cystic Cavity) Gomori's Aldehyde Fuchsin. × 85.

lateral or both these teeth. When the crown of the impacted tooth approaches the cervical region of the teeth to be retained, the palatal gingival attachments have been incised from premolar to premolar and the whole of the soft tissues of this region reflected. Since, in our experience, some pathology of the attachment tissues often followed this operation, despite the avoidance of excessive trauma and the careful replacement of the flap, and since such pathology is so frequently the forerunner of more serious trouble if neglected, we felt some experimental evidence might be helpful and therefore reflected the soft tissues in the two ways I have mentioned : first, by incising the crevicular epithelium and including the whole of the papillae in the flap and, secondly, by avoiding the papillae—the incision, in those cases, to be never nearer than 2mms. from the epithelial attachment.

The results of these two procedures confirm those of Mallett (1941) and Borden (1948) and clearly reveal that in the first instance the epithelial tissues always show some instability and often proliferation down the root surface and this, if not already pathological, is an ageing process and may subsequently result in a more serious condition.

In the second instance, that is avoiding the papillae and the crevicular epithelium, so long as the incision healed in a normal manner, there was no involvement of the epithelial attachment : where infection supervened the crevicular epithelium did in some instances become involved and proliferated into the connective tissues, presumably in response to Bier's "wound hormones." We did find, however, that provided the incision avoided the papillae by a sufficient margin, approximately 3mms., even delayed healing did not affect the epithelial attachment as shown in the other method.

Histologically a mucoperiosteal flap consists of stratified squamous epithelium overlying a relatively avascular collagenous lamina propria with limited elastic fibres. The periosteum is comprised of two layers, the external one being dense connective tissue with blood vessels, the internal one is more loosely arranged collagenous bundles, some of whose fibres enter the bone as Sharpey's fibres. The deeper layer also contains spindle shaped connective tissue cells and thin elastic fibres and its blood vessels are continuous with those of the external layer and penetrate the cortical plate of bone through Volkmann's canals to the Haversian Systems. In adult life, under normal conditions, the periosteum does not contain osteoblasts and it is only under *some stimulus such as an injury* that osteoblasts appear and bone is laid down.

In reflecting a flap, once an incision is made down to bone, the periosteum then strips away fairly readily as a thin avascular fibrous sheath, revealing, clinically at least, little continuity with the internal structure of the bone, and I, personally, have always wondered whether in fact it *is* an important link in the regenerative process or whether the alveolus would heal just as well without it.

In our teaching we always stress the need to carefully replace the flap against the cortical bone in order to avoid a large blood clot which is likely to become infected and, in any case, if extensive, is slow to organise. Sometimes some of the tooth is also reflected (Fig. 21).

When the periosteum does remain against the bone, its re-attachment takes place by a further deposition of a thin layer of bone on the surface of the cortical plate similar to periodontal membrane re-attachment to tooth surface by deposition of cementum and, contrary to the accepted belief in some quarters, exposure of this plate for up to one-and-a-half hours has not, as far as we could see, resulted in any damage to the bone.

You will remember, however, that prior to replacement of the flap in our surgical extractions, we incised the periosteum to permit the tissues to slide across the open wounds. Where this had been done there was at three days a considerable serous exudate which separated the flap from the bone. At twenty-one days bone formation was well established external to the cortical plate (Fig. 22) and by forty-seven days there was a very considerable formation of new bone in this region.

Fig. 21.

Fig. 22.

Fig. 21. Cementum and dentine removed from tooth in flap reflection. × 160.
Fig. 22. New bone external to cortical plate at twenty-one days. × 70.

When one comes to think of it, this really is not surprising for it is not dissimilar to what occurs in the fracture of a long bone and no doubt, given time, this new bone will become a part of the body of the mandible. It is an example of the periosteum's ability to produce osteoblasts in response to some stimulus, in this instance merely incision with a scalpel. This you will all agree is quite elementary histology and physiology, but it is something we would appear to have overlooked as a means of producing bone where it is needed.

It may be that somewhere here we will find the answer to our major problem of deficient alveolar bone and, with that goal in mind, we are proceeding further along these lines.

CONCLUSIONS

I feel sure you will appreciate the difficulties encountered in attempting to report four years research work in one lecture, and, because of the time factor, many details which I would have liked to illustrate have needed to be omitted. Of the work completed to date, the following conclusions seem justified :

1. So long as excessive force is not required, extraction of teeth with forceps, although leaving considerable blood clot exposed to the oral fluids, heals almost as rapidly and results in less reduction of alveolar bone and mucosal surface than with any other method of extraction.

2. Surgical removal of teeth with alveolectomy, involving loss of labial cortical bone, may result in early but not necessarily normal epithelialisa-

tion of the wound. It gives a relatively delayed return to normal of the bony architecture, alteration of contour and actual reduction of the alveolus and the mucosal surface.

3. Inter-septal alveolectomy with fracture of the buccal cortical plate without stripping of the mucoperiosteum, may also result in early but not necessarily normal epithelialisation, rapid obliteration of the reduced socket with new bone, but also gives alteration of the contour of the alveolus, not always for the better, and possibly reduction of the mucosal surface.

4. A surgical technique with minimal reflection of mucoperiostial tissues, removal of sufficient alveolar bone to permit ready elevation of teeth, careful apposition of freshened epithelial edges and immobilisation of flaps, gives a healing process approaching that of first intention healing. Under such conditions the remaining periodontal membrane, previously reported to be inactive in the regenerative process, does take an early and active part. Moderate surgical damage to the periosteum of the soft tissue flap results in deposition of lamellar bone external to the cortical plate.

5. In all methods of tooth removal, the earliest and the major contribution to bone formation comes from the cancellous bone surrounding the socket. Both the periodontal membrane and the periosteum play a comparatively minor part in this bony reconstruction.

6. Inclusion of the gingival tissues in mucoperiosteal flap reflection reduces the height of the epithelial attachment on the tooth concerned and may initiate parodontal disease ; the attachment is unaffected so long as the incision for reflection of a flap avoids the crevicular epithelium by a matter of 3mms.

ACKNOWLEDGMENTS

This lecture would indeed be incomplete without my referring to the part played by my colleagues, Mr. B. V. Janes and Mr. E. H. Seeley, in this investigation, for without their willing cooperation and assistance, none of it could have been accomplished.

My technician, Mrs. P. Harris, is responsible for the histological preparation and much of the photography.

We are also indebted to Professor G. A. G. Mitchell of the Anatomy Department of Manchester University for laboratory facilities, and the photographer of that Department, Mr. Howarth, has been most helpful in the production of the clinical photographs and criticism of our own efforts in this respect.

Dr. Ollerenshaw of the Medical Illustration Department provided the diagrams.

Finally, we are very much indebted to the Nuffield Foundation who have defrayed the major costs of the experimental work.

REFERENCES

BIER, A. (1917) *Dtsch. med. Wschr.* **43**, 833, 865, 897, 925.
BORDEN, S. M. (1948) *J. Canad. dent. Ass.* **14**, 510.
CHRISTOPHER, F. R. (1942) *Northw. Univ. Bull. dent. Res.* **43**, 7.
CLAFLIN, R. S. (1936) *J. Amer. dent. Ass.* **23**, 945.
EULER, H. (1923) *Dtsch. Mschr. Zahnheilk.* **41**, 685.
FLOREY, H. W. (1958) *General pathology*. London, Lloyd-Luke.
GLICKMAN, I., PRUZANSKY, S., and OSTRACH, M. (1947) *Amer. J. Orthodont.* (*Oral Surg. Sect.*) **33**, 263.
HARRIS, H. (1955) *Brit. J. exp. Path.* **36**, 454.
HARRISON, J. A. (1943) *The Bur* **43**, 107.
HUEBSCH, R. F., COLEMAN, R. D., FRANDSEN, A. M., and BECKS, H. (1952) *Oral Surg.* **5**, 864.
MALLETT, S. P. (1941) *Amer. J. Orthodont.* (*Oral Surg. Sect.*) **27**, 502.
MANGOS, J. F. (1941) *N.Z. dent. J.* **37**, 4.
MEYER, W. (1924) *Z. Stomatol.* **22**, 521.
SCHRAM, W. R. (1929) *J. Amer. dent. Ass.* **16**, 1987.
SIMPSON, H. E. (1958) *Brit. dent. J.* **104**, 99.
STEINHARDT, G. (1932) *Paradentium* **4**, 122.
SZABO, J. (1927) *Rev. Stomatol.* (*Paris*) **29**, 993.
VERSNEL, J. C. (1953) *J. Amer. dent. Ass.* **46**, 146.

CENTENARY CELEBRATIONS OF THE GRANTING OF THE ROYAL CHARTER BY MEANS OF WHICH THE LICENCE IN DENTAL SURGERY WAS INSTITUTED

22nd, 23rd and 24th July, 1959

PROGRAMME

Wednesday, 22nd July 1959

6.30 – 8.30 p.m. .. RECEPTION FOR FELLOWS AND LICENTIATES IN DENTAL SURGERY. Lounge suit. Admission by ticket

Thursday, 23rd July 1959

10.30 a.m. .. .. FORMAL OPENING

2.30 p.m. .. .. MENZIES CAMPBELL LECTURE by Professor Robert Bradlaw, C.B.E., F.R.C.S., F.D.S.R.C.S.ENG., entitled "Gaudeamus Igitur"

During the whole period of the Celebrations the Scientific Demonstrations will be on view, but throughout this day only demonstrators will be present to explain their exhibits. These Demonstrations will be staged by the Dental Schools in England.

7 for 7.30 p.m. .. L.D.S. CENTENARY FESTIVAL DINNER. Evening Dress and Decorations. Admission by ticket

Friday, 24th July 1959

10.30 a.m. .. .. ANNUAL GENERAL MEETING: PRESENTATION OF ADDRESSES: ELECTION OF A LICENTIATE TO THE BOARD OF FACULTY OF DENTAL SURGERY

2.30 – 4.30 p.m. .. SCIENTIFIC SYMPOSIUM—"TREATMENT OF THE CLEFT PALATE"

Chairman: Sir William Kelsey Fry, C.B.E., M.C., F.R.C.S., F.D.S.R.C.S.ENG.

Speakers: Mr. W. R. Burston, L.D.S.(L'pool), D.ORTH., R.C.S.ENG.—"Development"

Sir Archibald McIndoe, C.B.E., F.R.C.S.—"Cleft Palate Surgery"

Mr. D. F. Glass, L.D.S.R.C.S.ENG., D.D.O., R.F.P.S.GLAS.—"Orthodontic Treatment"

Mr. K. P. Liddelow, F.D.S.R.C.S.ENG., H.D.D.R.C.S.ED.—"Prosthetic Treatment"

(Time will be allowed for questions)

6.00 – 7.30 p.m. .. RECEPTION AT SENATE HOUSE, UNIVERSITY OF LONDON. Lounge suits. Admission by ticket.

THE PATHOLOGY OF HYDROCEPHALUS

Erasmus Wilson Demonstration delivered at the Royal College of Surgeons of Engla
on
23rd October 1958
by

K. M. Laurence, M.A., M.B., Ch.B.
Department of Morbid Anatomy, The Hospital for Sick Children, Great Ormond Stree *

ERASMUS WILSON, APART from being an eminent dermatologist of the latter end of the last century, and a past President of this College, was also a keen Egyptologist. I am sure that had he been fortunate enough to discover the hydrocephalic mummy of the Roman period reported by Douglas Derry in 1913, his interest in hydrocephalus might well have been aroused.

Today, I would like to discuss the naked eye pathology of hydrocephalus, and shall base this talk on post-mortem material obtained during my tenure of the Hydrocephalus Research Fellowship at The Hospital for Sick Children, Great Ormond Street. Most of these cases were examined using a special technique first described by Martin (1952) which was later modified (Laurence and Martin, 1959) whereby the brain is allowed to fix *in situ* within the skull several weeks before a dissection is made. This not only permits grossly hydrocephalic brains to be examined without danger of distortion, but it enables minor degrees of malformation and abnormality to be recognised, some of which would undoubtedly have been missed if conventional methods of removing the brain from the bony cage were employed. Most important of all, this method allows the careful examination of the extra-cerebral cerebro-spinal fluid pathways, such as the basal cisterns, almost impossible by any other method.

Hydrocephalus is best defined as the excessive accumulation of cerebro-spinal fluid within the cranial cavity. I wish, however, to exclude hydrocephalus *e vacuo* where an excessive amount of cerebro-spinal fluid replaces volume lost through primary atrophy of the brain.

Theoretically, hydrocephalus may be brought about in three separate ways (see Table I).

TABLE I

CAUSES OF HYDROCEPHALUS

Over-production of C.S.F.	..	Choroid plexus papilloma and villous hypertrophy.
Defective absorption of C.S.F.	..	? ? Venous sinus thrombus.
Obstruction to the C.S.F. pathway		*Within ventricular system:* Foramina of Monro; Aqueduct; Exit foramina
		Subarachnoid space : Arnold-Chiari malformation; Basal cistern block
		Outside C.N.S.: Skull abnormalities

Over-production of cerebro-spinal fluid

That over-production of cerebro-spinal fluid occurs is now conceded by most authorities (Russell, 1954). The choroid plexus papillomata, in which

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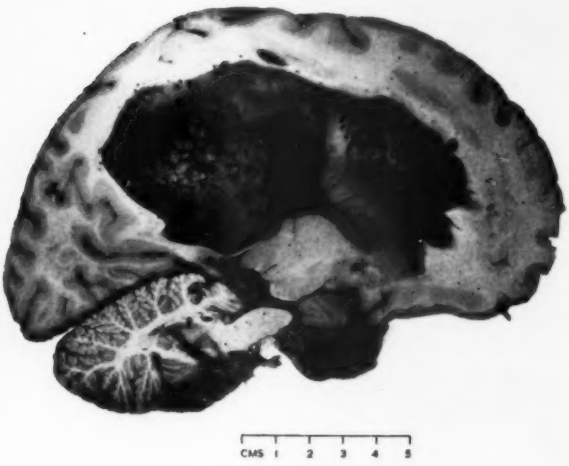

Fig. 1. A parasagittal section through a brain to show a large choroid plexus papilloma situated in the posterior portion of the markedly dilated lateral ventricle. The tumour is attached to the tela choroidea anteriorly, as well as to the ventricular wall by a secondary glial stalk posteriorly. The subependymal haemorrhages are a terminal event.

this is seen, form about 3 per cent. of childhood intra-cranial tumours. The cauliflower-like tumour, friable and vascular, is attached to the choroid plexus and is usually situated in the posterior portion of a lateral ventricle and the whole ventricular system is symmetrically and often markedly dilated (Fig. 1). Microscopically most of these tumours, although more vascular, have the normal structure. One would therefore expect such a tumour to be functional and by virtue of its bulk to secrete excessive amounts of cerebro-spinal fluid. Such functional activity is well known in a number of types of tumour. The absence of obstruction to the flow of cerebro-spinal fluid has been demonstrated in a number of cases, including one of this series, not only by encephalography when air is found to pass from the basal cisterns into the Sylvian fissures, but also at autopsy when even in the presence of considerable hydrocephalus, a comparatively wide and almost normal cerebro-spinal fluid-filled subarachnoid space is sometimes seen. However, in an appreciable number of cases, although no obstruction is found, the meninges are opaque and considerably thickened. Whether this is due to the effect of a high protein in the cerebro-spinal fluid, which is usually associated with such a tumour, or due to a compensatory hypertrophy from a high cerebro-spinal fluid pressure, analogous to the hypertrophy of blood vessels

in hypertension, is not easy to decide. A more likely explanation for this meningeal thickening might be, that repeated minor haemorrhages, known to occur from these vascular papillomas, set up a reactive fibrosis. This would be supported by the finding of basal cistern block in an appreciable proportion of such cases.

Under-absorption

Theoretically, under-absorption of cerebro-spinal fluid would be brought about by obstruction of the venous return as in venous sinus thrombosis. This, however, is not well authenticated, and in every case of thrombosis that I have had the opportunity of examining, I was able to find another cause for the hydrocephalus.

Obstruction of the cerebro-spinal fluid pathway

This group is numerically and pathologically the most important. Before considering it in detail I would like to restate the general principle that proximal to the site of obstruction the cerebro-spinal fluid pathway becomes dilated. Thus, if the lateral and third ventricles are dilated and the fourth ventricle is of normal dimensions, the obstruction is likely to be situated within the aqueduct of Sylvius; when the whole of the ventricular system is dilated but the basal cisterns are of normal size, then the block will be found at the exit foramina of the fourth ventricle.

If, on the other hand, the whole ventricular system and the basal cisterns are dilated, then a basal cistern block is likely to be the cause of the hydrocephalus. As there are two sets of choroid plexi, one set within the lateral and third ventricles, and another choroid plexus within the fourth ventricle, dilatation may take place below an aqueduct block if an additional block in the fourth ventricle or the basal cisterns is present.

MALDEVELOPMENTS

Malformation of the aqueduct of Sylvius

Before considering the malformation of the aqueduct a brief consideration of its normal structure will be of help. The aqueduct is a channel linking the third and fourth ventricles, normally about 11mm. in length and 0.9sq.mm. in average minimum cross-sectional area (Woollam and Millen, 1953). It is completely lined by ependyma and is surrounded by normal brain tissue without gliosis.

Two malformations have to be considered, namely stenosis and forking. The former, stenosis, is an uncommon condition which may be associated with other cerebral malformations. Here the normal shape of the aqueduct is sometimes preserved but the aqueduct is of markedly reduced diameter, but often it has a crenated and irregular outline. The ependymal lining, however, remains intact and the surrounding brain tissue is normal and free from excessive gliosis.

Forking of the aqueduct on the other hand is a fairly common anomaly frequently associated with the Arnold-Chiari malformation. Here, the aqueduct usually divides into a large dorsal and a number of smaller

ventral channels, each generally irregular in outline but with an intact ependymal lining. These channels have a greatly reduced combined cross-sectional area. Normal brain tissue, free from gliosis, intervenes between them.

Spina bifida with hydrocephalus

This is the largest and most important group of malformations associated with hydrocephalus and, before dealing with the hydrocephalus itself, I must briefly review the anatomy of spina bifida.

In spina bifida occulta, the mildest abnormality of the group, the spines have failed to fuse. The spinal cord, with its meninges, remains within the spinal canal. Frequently, overlying skin shows abnormalities. The spinal cord may show abnormalities which lead to the associated weaknesses of the legs and urinary troubles sometimes found.

A meningocoele is a lesion where accompanying the spina bifida the meninges have herniated out of the spinal canal, and are to be found directly on the surface or covered with abnormal or normal skin. The cord remains within the spinal canal, but may show a variety of malformations (Cameron, 1956). Myelocoeles and myelomeningocoeles are essentially the same lesion. Here, the neural tube has failed to close early in inter-uterine life and the neural plate remains on the surface. At birth the neural plate is seen as a raw, apparently ulcerated area surrounded by a blue, transparent membrane, representing the meninges. In the fortunate cases the myelocoele will epithelialise over from the surrounding skin in seven to ten days. More frequently, however, the neural plate becomes infected and healing takes place after much fibrosis and scarring, and finally the whole lesion may become well epithelialised. Thus, the typical spina bifida cystica of bizarre shape develops.

Meningocoeles are comparatively rare—only about 5 per cent. of the cases seen at The Hospital for Sick Children prove to be true meningocoeles and I have not, so far, had the opportunity of examining such a case in the post-mortem room, for they carry a very hopeful prognosis regarding life. The majority of cases are myelocoeles, and nearly all of these are associated with some form of malformation of the hind-brain ; a small proportion of those in whom the myelocoele is situated very low down the cerebral spinal axis forming the exception. The hind-brain abnormality generally takes the form of an Arnold-Chiari malformation (Fig. 2). This consists of the Arnold malformation, where the cerebellum is often small and poorly lobated, with a midline tongue consisting of vermis which extends for a variable distance down the spinal canal, and the Chiari malformation, where an elongated medulla extends for a variable distance beyond the level of the foramen magnum. In addition the medulla is frequently kinked backwards upon the cord. Lying between the cerebellum and the pons and medulla is a long and often narrow fourth ventricle, the choroid plexus of which generally forms a compact mass near the tip of the cerebellar prolongation. Sometimes there is an

Fig. 2. A hemisected skull and spinal cord showing the Arnold-Chiari malformation. The elongated medulla (Chiari malformation) is not only largely intraspinal, but is also kinked upon the cord. A well developed cerebellar tongue (Arnold malformation) is shown. The myelocoele in the lumbo-sacral region is typical, with nerve roots leaving the neural plate to gain the root canals. The cord shows slight hydromyelia.

extension of the fourth ventricle within the medulla beyond the exit foramina. In all but the mildest cases the upper spinal nerve routes take a cranial course. The whole is generally covered by congested meninges. This congestion in time will lead to thickening and fibrosis. The malformation may be only very slight, measuring 3 or 4mm., and thus easily missed if the brain is removed and examined by the conventional methods, while in other cases the Chiari malformation alone may be present. Here, a lengthened medulla extends for a variable distance down the spinal canal, but the cerebellum is relatively normal.

The Arnold-Chiari malformation must be differentiated from a tonsillar herniation. In the latter the tonsils descend down the spinal canal laterally, while in the Arnold-Chiari malformation it is the vermis which extends in the midline, posteriorly. Moreover, in the tonsillar herniation, there is no medullary component.

Associated with the malformation of the hind-brain, other congenital deformities, especially of the central nervous system, are frequently found. Aqueduct forking has already been mentioned. The thalamic bodies may be fused to a variable degree, leading to a large inter-thalamic bar or massa intermedia. Micro-gyrations are frequently present, and a hypoplastic falx and great longitudinal fissure are also common, together with inter-digitation between the two cerebral hemispheres. Ectopic subependymal grey matter is sometimes seen, while in many cases there is upward herniation of the cerebellum through the tentorial opening and hydromyelia and diastomatomyelia of the cord. Frequently renal and skeletal malformations are also found. These are only some of the anomalies that may be present.

Space will not permit a discussion of the aetiology of these malformations, which are adequately discussed by Cameron (1957), but the aetiology of the associated hydrocephalus is of prime importance here. Aqueduct abnormalities will, in themselves, lead to hydrocephalus; so will the Arnold-Chiari malformation by virtue of the crowding of structures in the often small posterior fossa and in the upper spinal canal. The hyperaemia and eventual fibrosis and thickening of the meninges surrounding the Arnold-Chiari malformation may further interfere with an already embarrassed cerebro-spinal fluid circulation. Most important of all, however, is the effect of an ascending infection from the raw spina bifida cystica leading to post-inflammatory obstructions. Thus, a block of the foramina of Monro (Fig. 3), aqueduct block, blocks of the exit foramina or basal cistern block may be superimposed upon any congenital malformations that may be present.

Septum formation in the aqueduct, foramina of Monro and exit foramina of the fourth ventricle is exceedingly rare, and I have not had the opportunity to dissect a case. Nor have I had the opportunity to examine skeletal abnormalities such as an achondroplasia leading to hydrocephalus.

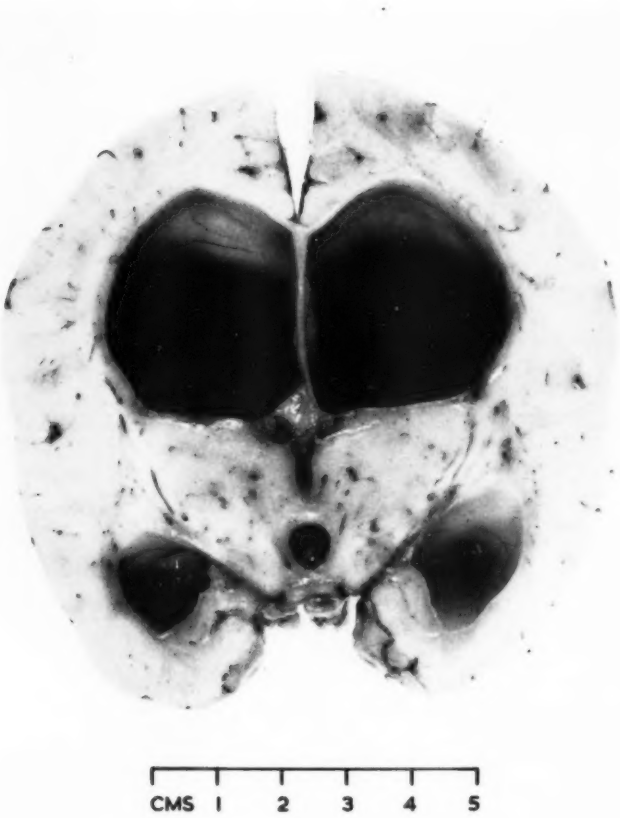

Fig. 3. A coronal section of the cerebral hemispheres showing a post-inflammatory block of the foramina of Monro following an ascending infection from a myelocoele. A large interthalamic connexus is also present.

GLIOSIS OF THE AQUEDUCT

Gliosis is an interesting and controversial group as there has been much discussion about the aetiology of this condition. Here, the aqueduct is narrowed, subdivided or completely occluded by an overgrowth of subependymal fibrillary neuroglia (Fig. 4). The outline of the original aqueduct is marked out by disorderly islets of ependymal cells left behind by the gliosis (Fig. 5). If a central channel remains this rarely has any ependymal lining. Clinically, hydrocephalus begins insidiously, often somewhat later in childhood or even in early adult life, and there is never any history suggestive of an antecedent infection.

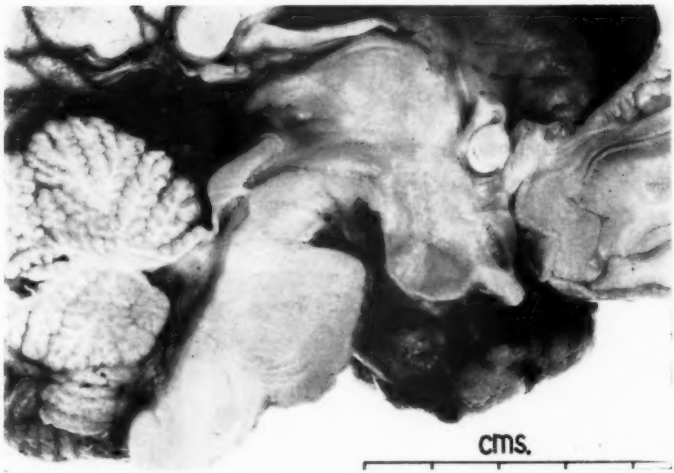

Fig. 4. A midline section showing the aqueduct completely occluded by gliosis in a case associated with neurofibromatosis. The lateral and third ventricles are grossly dilated.

Fig. 5. Transverse section through an aqueduct showing gliosis. (Mallory's phosphotungstic acid haematoxylin. × 18)

Spiller (1916) suggested that the condition might be due to an involutional hyperplasia of the subependymal glia, analagous to the closing off of the central canal of the spinal cord that occurs in the second decade while others have favoured an inflammatory origin on its similarity to post-inflammatory gliosis (Russell, 1949). I have had the opportunity of examining four cases of gliosis in which the condition was associated with neurofibromatosis. The latter is well known, being a hereditary and familial condition which would appear to be a system defect of the neuroectodermal elements of the central and peripheral nervous system, regarded by Willis (1948) as hamartomatous. Optic nerve " gliomas " also regarded as hamartomatous (Crome, 1954) are a common complication in such cases, while blastoma-like microscopic foci have been found scattered in the glial tissue (Scharenberg, 1953). On the other hand tumour involvement of the brain (Turner and Gardner, 1938) (which may have arisen in such a hamartomatous area) is well known. The aqueduct gliosis in these four examples of neurofibromatosis may also be of hamartomatous origin, a view supported by finding nests of bizarre glial cells in the peri-aqueductal tissues. I would like to suggest that aqueduct gliosis unassociated with neurofibromatosis may also have the same origin.

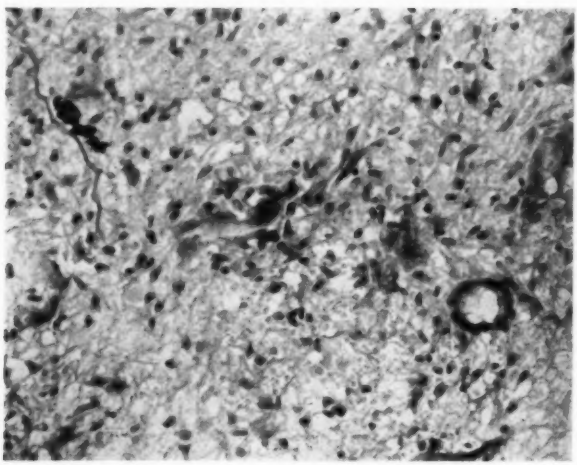

Fig. 6. Photomicrograph of the peri-aqueductal glial tissue to show bizarre cells, including multinucleate forms. (Haematoxylin and Van Gieson. × 180)

INFLAMMATIONS

This is a large and important group, and one of the commonest causes of post-inflammatory hydrocephalus is blood in the cerebro-spinal fluid pathway. This generally results from birth trauma, especially in premature and first-born infants. It has recently been made abundantly clear that

to produce such trauma the delivery need not have been at all remarkable and that the infant need show no signs specifically associated with intracranial mischief (Bound, Butler and Spector, 1956). It is worth remembering that when a subdural haematoma is found the injury responsible for this has very likely produced bleeding into the cerebro-spinal fluid as well. Also, the same birth injury may well have produced parenchymal brain damage in addition. However, bleeding into the cerebro-spinal fluid pathway resulting from haemorrhage from berry aneurysms, following operations or head injuries in childhood, may also give rise to hydrocephalus (Foltz and Ward, 1956).

Infections form the other important inflammatory group. These infections may be either acute or chronic, of bacterial, and less frequently of viral or toxoplasmal origin. Often the mild and missed infections produce the worst effects, as such cases receive only late treatment or may receive none at all. On the other hand an E. coli meningitis in the neo-

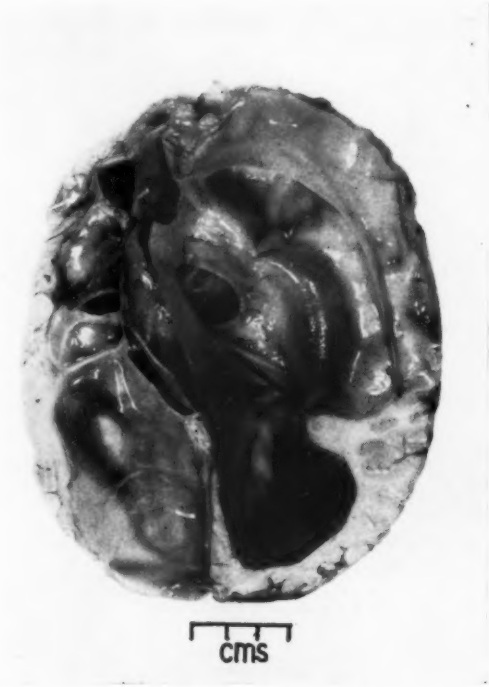

Fig. 7. Horizontal section through the cerebrum of a case of hydrocephalus following B. coli meningitis. The lateral ventricles have been converted into a series of intercommunicating cysts.

natal period may also be completely silent. With all these infections parenchymal brain damage is common.

A variety of anatomical lesions may follow these inflammations. The most severe effects, often resulting from an E. coli meningitis, may lead to an organising pyocephalus. Here, the whole ventricular system may be converted into a series of intercommunicating cysts, and the foramina of Monro may also become occluded (Fig. 7). In the less severe inflammations, the aqueduct, always a vulnerable structure in view of its position and narrowness, may become blocked. This block may result from its lumen being occluded by pus or a small blood clot. On the other hand the block may follow from damage to its ependymal lining; the ependyma is very delicate and once it is damaged or denuded it will not regenerate, the subependymal glia then proliferates and may finally completely occlude the channel. In the majority of cases, however, an inflammatory reaction occurs in the meninges, leading to occlusive fibrosis there. This process may

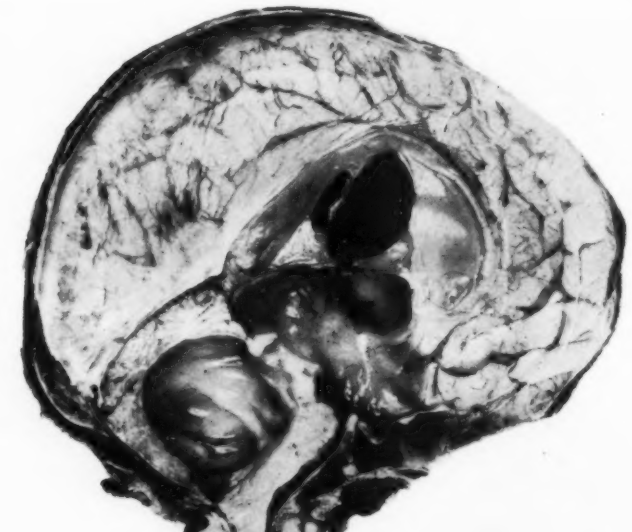

Fig. 8. Midline section through the skull showing a hugely dilated ventricular system due to a block at the exit foramina of the fourth ventricle. Note the inconspicuous basal cisterns and the ballooned floor of the third ventricle.

Fig. 9. Midline section through a skull showing a basal cistern block. The third and fourth ventricles are enormously dilated. Fine fibrous strands traverse the cisterns. The interpeduncular cistern has so greatly expanded as to elevate the floor of the third ventricle, elongate the optic nerve and the pituitary stalk and flatten the pituitary gland.

cause a block of the exit foramina of the fourth ventricle, for the arachnoid may become bound down in their immediate vicinity (Fig. 8). In other cases the foramina remain clear, but the arachnoid becomes bound down on the edge of the basal cisterns and thus gives rise to a basal cistern block. The cisterns then tend to dilate, compressing the cerebellum, elevating the floor of the third ventricle, or stretching the optic nerve and the pituitary stalk (Fig. 9).

Any combination of all these inflammatory lesions may be present in a particular case. Thus, a case of inflammatory aqueduct stenosis may well be associated with a block at the exit foramina or the basal cisterns as well.

Tumours

Tumours in any position may give rise to obstructive hydrocephalus. A six week old infant, for example, who had apparently a congenital aqueduct block, was found subsequently at post-mortem to have cerebellar medulloblastoma compressing that structure.

In conclusion I shall consider the aetiology of the hydrocephalus in the hundred consecutive post-mortems carried out at The Hospital for Sick Children and at the Westminster Children's Hospital on which this paper is based. (The numbers shown in Figures 3 and 4 are, however, only provisional, as the data on all these cases is not yet entirely complete). It

TABLE II

AETIOLOGY OF HYDROCEPHALUS
(100 Post-mortem examinations)

Malformation:		46
Alone	14	
With infection	30	
With trauma	2	
Inflammation:		50
Infection alone	17	
Trauma alone	22	
Unknown (probably infection or trauma)	11	
Tumours		4

is seen from Table II that in almost half the cases a malformation was the basis, though in the majority of these the malformation was associated with a super-added inflammatory lesion. In the case where the hydrocephalus was of purely inflammatory origin, trauma, and in nearly all instances birth trauma, accounted for a large proportion. This is in agreement with results obtained in another investigation where almost one-third of all the cases in the series had this aetiology (Laurence, 1958). In eleven cases it was impossible to decide on the evidence available which of the two main inflammatory aetiologies was responsible. In four cases a tumour was found to be the underlying cause of the disease. In all these four the tumour was an unexpected finding.

TABLE III

SITE OF BLOCK CAUSING HYDROCEPHALUS
(100 Post-mortem examinations)

Isolated sites:		50
Aqueduct	10	
IV Ventricle foramina	7	
Basal cistern block	21	
Arnold-Chiari malformation	12	
Multiple sites:		48
Basal cistern block	20	
With block at foramina of Monro, aqueduct or IV ventricle.		
Arnold-Chiari malformation	28	
With blocks at foramina of Monro, aqueduct, IV ventricle or basal cistern.		
No block (over-secretion) :		2

Table III shows that an anatomical cause for the hydrocephalus was found in every case examined, though two children had hydrocephalus due to over-secretion of fluid. It is interesting to note that about half the cases had more than one site of block.

ACKNOWLEDGMENTS

I am indebted to Mr. D. Martin and the staff of the Department of Medical Illustration for the illustrations and preparations of the specimens, diagrams and charts shown in the demonstration, which accompanied this lecture. Thanks are due to the Research Committee of The Hospital for Sick Children, Great Ormond Street, and especially Dr. M. Bodian and Mr. G. H. Macnab for their help, encouragement and support, and to Professor G. J. Cunningham for his part in enabling me to give this lecture-demonstration.

REFERENCES

BOUND, J. P., BUTLER, N. R., and SPECTOR, W. G. (1956) *Brit. med. J.* **2**, 1191 and 1260.
CAMERON, A. H. (1956) *Lancet* **2**, 171.
——— (1957) *J. Path. Bact.* **73**, 195 and 213.
CROME, L. (1954) *J. Path. Bact.* **67**, 407.
CROWE, W. F., SCHULL, W. F., and NEEL, J. V. (1956) *Multiple neurofibroma.* Springfield, Ill., U.S.A.
DERRY, D. E. (1912-13) *J. Anat. (Lond.)* **47**, 436.
FOLTZ, E. L., and WARD, A. W. (1956) *J. Neurosurg.* **13**, 546.
LAURENCE, K. M. (1958) *Lancet* **2**, 1152.
——— and MARTIN, D. (1959) *J. clin. Path.* **12**, 188.
MARTIN, D. (1952) *Med. biol. Ill.* **2**, 260.
RUSSELL, D. S. (1949) *M.R.C. Spec. Rep. Ser., No.* 265. London.
——— (1954) *Ass. Res. nerv. Dis. Proc.* **34**, 161.
SPILLER, W. G. (1916) *J. nerv. ment. Dis.* **44**, 395.
TURNER, C. A., and GARDNER, W. D. (1938) *Amer. J. Cancer* **32**, 339.
WILLIS, R. A. (1948) *Pathology of tumours.* London, Butterworth, p. 838.
WOOLLAM, D. H. M., and MILLEN, J. W. (1953) *Brain* **76**, 104.

PROCEEDINGS OF THE COUNCIL IN MAY

AT A MEETING of the Council on the 14th May, with Professor Sir James Paterson Ross, President, in the Chair, Mr. E. D. Ahern, Brisbane, and Dr. John H. Gibbon, Philadelphia, were admitted to the Hon. Fellowship.

The Lady Cade Medal was awarded to Squadron Leader T. C. D. Whiteside for his research on the effect, on visual performance, of dazzle from sources of very high brightness.

The Begley Prize was awarded to Dr. Geoffrey S. Makin of Liverpool University.

Diplomas of Membership were granted to 147 candidates and one diploma of Fellowship was granted.

Diplomas were granted, jointly with the Royal College of Physicians, as follows: *Physical Medicine* (1); *Tropical Medicine and Hygiene* (2).

It was reported that the College of General Practitioners, which had hoped to erect a building in Lincoln's Inn Fields, had now been prevented from doing so by a series of setbacks, the most significant of which were the town planning conditions and difficulties over security of tenure.

The following hospitals were recognised under paragraph 23 of the F.R.C.S. regulations:

HOSPITALS	POSTS RECOGNISED		
	General (6 mths. unless otherwise stated)	Casualty (all 6 mths.)	Unspecified (all 6 mths.)
BATH — St. Martin's Hospital (additional)	H.S. (S.H.O.)		
BATH — Royal United Hospital (additional)	H.S. (S.H.O.)		
LANCASTER—Beaumont Hospital and Lancaster Royal Infirmary (additional)			*Under para* 23 (*c*) *Temporary recognition for one year* S.H.O. (E.N.T.)
LONDON — Connaught Hospital, Walthamstow		*Change of recognition of* Casualty Registrar and Deputy Resident Surgical Officer from 6mths. unspecified to 6mths. Casualty.	

Hospitals	Posts Recognized		
	General (6mths. unless otherwise stated)	Casualty (all 6mths.)	Unspecified (all 6mths.)
Grimsby—Grimsby and District Hospitals (Redesignation)	*Redesignation of* R.S.O. (J.H.M.O.) at Louth County Infirmary as Registrar		
Woking and Chertsey Group ..		*Change of recognition from* Cas. Off. St. Peter's Chertsey (6mths.) to Cas. Off. St. Peter's Chertsey and Woking Victoria Hospital (6mths.)	
Lancaster — Royal Infirmary (additional)			Regr. (Orth.)
London — Prince of Wales's General Hospital (additional)		Res. Orth H.S. and Sen. Cas. Off. (S.H.O. grade)	
Guildford — Royal Surrey County Hospital (additional)		Orth. H.O. (Casualty)	
London — Whittington Hospital (additional)		Cas. Off. (J.H.M.O.) 3 Cas. Offs. (S.H.O.)	
Blackpool — Victoria Hospital (additional)	Regr. (6mths.)	and present post of R.S.O. reduced from 12 to 6mths.	
Alton—General Hospital (additional)	Regr. or H.S.		
Sydney—Royal South Sydney Hospital	H.S.		
Royal Naval Hospitals.. ..	Redesignation and reorganisation of posts		
	Formerly recognised		
R.N. Hospital, Chatham ..	Surg. Spec. Asst. Surg. Spec.		Gen. Surg. & Orth. Spec. Asst. Gen. Surg. & Orth. Spec. Urologist Asst. Urologist
R.N. Hospital, Haslar	Surg. Spec. Asst. Surg. Spec.		Orth. Spec. 2 Asst. Orth. Specs. Urologist Asst. Urologist
R.N. Hospital, Plymouth ..	Sen. Surg. Spec. Asst. Surg. Spec.		Orth. Spec. Asst. Orth. Spec. Urol. Spec. Asst. Urologist
	Now recognised		
R.N. Hospital, Haslar	3 S.H.O.'s	Cas. Off.	2 S.H.O.'s (Orth. & Gen.)
R.N. Hospital, Plymouth ..	2 S.H.O.s	Cas. Off.	1 S.H.O. (Orth. & Gen.)
R.N. Hospital, Chatham ..	2 S.H.O.s	Cas. Off.	1 S.H.O. (Orth. & Gen.)

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£10,000	F. R. Moser, L.D.S.R.C.S.—for the endowment of the Quintin Hogg Fellowship
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DIARY FOR JUNE

Tues. 16		Names of candidates (L.D.S.) for election to the Board of Faculty of Dental Surgery announced.
Wed. 17		Primary F.F.A. Examination begins.
	5.00	Board of Faculty of Anaesthetists.
Thur. 18		Pre-Medical Examination D.L.O. Examination (Part I) and D.P.M. Examination (Part II) begin.
Fri. 19		Election of Fellows to the Board of Faculty of Dental Surgery. Dental Lectures and Clinical Conferences end.
Thur. 25		First Membership Examination and D.L.O. Examination (Part II) begin.
Tues. 30		Final Membership Examination begins.

DIARY FOR JULY

Thur. 2	11.00	Election to Council.
	5.30	DR. D. HILL—Otolaryngology Lecture—The value of the electro-encephalography in diagnosis.*
Tues. 7		Final F.D.S. Examination begins.
Wed. 8		First L.D.S. Examination begins.
	5.00	DR. J. E. DUNPHY—Moynihan Lecture—On the nature and care of wounds.*
Thur. 9		Election of President, Vice-Presidents, and Lecturers.
	10.30	QUARTERLY COUNCIL.
Fri. 10	5.00	MR. E. M. NANSON—Hunterian Lecture—Tumours of the parotid gland.*
Wed. 15		D.O. Examination and D.T.M. & H. Examination begin.
Thur. 16		Final F.F.A. Examination, D.I.H. Examination, and D.Phys.Med. Examination (Part I) begin.
Thur. 23		D.Phys.Med. Examination (Part II) begins.
	10.30	Centenary Celebrations of the Granting of the Royal Charter by means of which the Licence in Dental Surgery was Instituted.
	2.30	PROF. R. BRADLAW—Menzies Campbell Lecture—Gaudeamus Igitur.* During the whole period of the Celebrations the Scientific Demonstrations will be on view but throughout this day only demonstrators will be present to explain their exhibits. These Demonstrations will be staged by the Dental Schools in England.
Fri. 24	10.30	Annual General Meeting of Faculty of Dental Surgery; Presentation of Addresses; Election of a Licentiate to the Board of Faculty of Dental Surgery.
	2.30	Scientific Symposium—Treatment of the cleft palate.* Chairman: SIR WILLIAM KELSEY FRY. Speakers: W. R. BURSTON—Development. SIR ARCHIBALD MCINDOE—Cleft palate surgery. D. F. GLASS—Orthodontic treatment. K. P. LIDDELOW—Prosthetic treatment.
		Basic Sciences Lectures and Demonstrations for Dental Students end.
Thur. 30	2.00	ORDINARY COUNCIL.

*Not part of course.

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